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(54) Title: METHODS FOR TREATING GENETICALLY-DEFINED PROLIFERATIVE DISORDERS WITH HSP90 INHIBITORS

Type of Aberration	Background Literature	Affected Gene(s)	Protein Domain	Fusion Protein	Disease
t(9; 22)(q34; q11)	de Klein, A. et al. Nature 300, 765-767 (1982)	<i>CABL</i> (9q34) <i>BCR</i> (22q11)	tyrosine kinase serine kinase	serine + tyrosine kinase	CML/ALL
inv14 (q11; q32)	Baer, R., Chen, K.-C., Smith, S. D. & Rabbitts, T. H. Cell 43, 705-713 (1985); Denny, C. T. et al. Nature 320, 549-551 (1986)	TCR- $\alpha$ (14q11) VH- (14q32)	TCR- $\alpha$ Ig VH	VH-TCR- $\alpha$	T/B-cell lymphoma
t(1; 19)(q23; p13.3)	Kamps, M. P., Murre, C., Sun, X.-H. & Baltimore, D. Cell 60, 547-555 (1990); Nourse, J. et al. Cell 60, 535-545 (1990)	<i>PBX1</i> (1q23) <i>E2A</i> (19p13.3)	HD AD-b-HLH	AD + HD	pre-B-ALL
t(17; 19)(q22; p13)	Hunger, S. P., Ohyashiki, K., Toyama, K. & Clearly, M. L. Genes Dev. 6, 1608-1620 (1992); Inaba, T. et al. Science 257, 531-534 (1992)	<i>HLF</i> (17q22) <i>E2A</i> (19p13)	bZIP AD-b-HLH	AD + bZIP	pro-B-ALL
t(15; 17)(q21-q11-22)	Giliard, E. F. & Solomon, E. Sem. Cancer Biol. 4, 359-368 (1993)	<i>PML</i> (15Q21) <i>RARA</i> (17q21)	Zinc-finger Retinoic acid receptor- $\alpha$	Zinc-finger + RAR DNA and ligand binding	APL
t(11; 17)(q23; q21.1)	Chen, Z. et al. EMBO J. 12, 1161-1167 (1993)	<i>PLZF</i> (11q23) <i>RARA</i> (17q21)	Zinc-finger Retinoic acid receptor $\alpha$	Zn-finger + RAR DNA and ligand binding	APL
t(4; 11)(q21; q23)	Djabali, M. et al. Nature Genet. 2, 113-118 (1992); Gu, Y. et al. Cell 71, 701-708 (1992)	<i>MLL</i> (11q23) <i>AF4</i> (4q21)	A-T hook/Zn-finger Ser-Pro rich	A-T hook + (Ser-pro)	ALL/pre-B-ALL/ ANLL
t(9; 11)(q21; q23)	Nakamura, T. et al. Proc. natn. Acad. Sci. U.S.A. 90, 4631-4635 (1993); Lida, S. et al. Oncogene 8, 3085-3092 (1993)	<i>MLL</i> (11q23) <i>AF9/MLLT3</i> (9p22)	A-T hook/Zn-finger Ser-Pro rich	A-T hook + (Ser-Pro)	ALL/pre-B-ALL/ ANLL
t(11; 19)(q23; p13)	Tkachuk, D. C., Kohler, S. & Cleary, M. L. Cell 71, 691-700 (1992); Yamamoto, K. et al. Oncogene 8, 2617-2625 (1993)	<i>MLL</i> (11q23) <i>ENL</i> (19p13)	A-T hook/Zn-finger Ser-Pro rich	A-T hook + Ser-Pro	pre-B-ALL/ T-ALL/ ANLL

(57) Abstract: The invention relates generally to methods of treating cell proliferative diseases with HSP90 inhibitors and, depending on the specific aspect and embodiment(s) claimed, to the treatment of proliferative diseases that are associated with fusion proteins, e.g., bcrabl, or mutant proteins or cellular protein isoforms, e.g., mutant forms of p53.



WO 02/069900 A2

## Methods for Treating Genetically-Defined Proliferative Disorders with HSP90 Inhibitors

### Field of the Invention

The field of the invention relates to chemotherapeutic treatments of proliferative disorders, including rheumatoid arthritis and neoplasias.

### Background of the Invention

The following description includes information that may be useful in understanding the present invention. It is not an admission that any of the information provided herein is prior art, or relevant, to the presently claimed inventions, or that any publication specifically or implicitly referenced is prior art.

The eukaryotic heat shock protein 90s (HSP90s) are ubiquitous chaperone proteins that are involved in folding, activation and assembly of a wide range of proteins, including key proteins involved in signal transduction, cell cycle control and transcriptional regulation. HSP90 proteins are highly conserved in nature (see, e.g., NCBI accession # P07900 (SEQ ID NO: 318) and XM004515 (SEQ ID NOs: 319 and 320) (human  $\alpha$  and  $\beta$  HSP90, respectively), P11499 (SEQ ID NO: 321) (mouse), AAB23369 (SEQ ID NO: 322) (rat), P46633 (SEQ ID NO: 323) (chinese hamster), JC1468 (SEQ ID NO: 324) (chicken), AAF69019 (SEQ ID NO: 325) (fleshfly), AAC21566 (SEQ ID NO: 326) (zebrafish), AAD30275 (SEQ ID NO: 327) (salmon), AAC48718 (SEQ ID NO: 328) (pig), NP 015084 (SEQ ID NO: 329) (yeast), and CAC29071 (SEQ ID NO: 330) (frog).

Researchers have reported that HSP90 chaperone proteins are associated with important signaling proteins, such as steroid hormone receptors and protein kinases, including many that are implicated in tumorigenesis, e.g., Raf-1, EGFR, v-Src family kinases, Cdk4, and ErbB-2 (Buchner J., 1999, *TIBS*, 24:136-141; Stepanova, L. *et al.*, 1996, *Genes Dev.* 10:1491-502; Dai, K. *et al.*, 1996, *J. Biol. Chem.* 271:22030-4). *In vivo* and *in vitro* studies indicate that certain co-chaperones, e.g., Hsp70, p60/Hop/Sti1, Hip, Bag1, HSP40/Hdj2/Hsj1, immunophilins, p23, and p50, may assist HSP90 in its function (Caplan, A., 1999, *Trends in Cell Biol.*, 9: 262-68).

Ansamycins are antibiotics derived from *Streptomyces hygroscopicus* which are known to inhibit HSP90s. These antibiotics, e.g., herbimycin A (HA) and geldanamycin (GM), as well as other HSP90 inhibitors such as radicicol, bind tightly to an N-terminal pocket in HSP90 (Stebbins, C. *et al.*, 1997, *Cell*, 89:239-250). This pocket is highly conserved and has weak

homology to the ATP-binding site of DNA gyrase (Stebbins, C. *et al.*, *supra*; Grenert, J.P. *et al.*, 1997, *J. Biol. Chem.*, 272:23843-50). ATP and ADP have been shown to bind this pocket with low affinity, and HSP90 itself has been shown to have weak ATPase activity (Proromou, C. *et al.*, 1997, *Cell*, 90: 65-75; Panaretou, B. *et al.*, 1998, *EMBO J.*, 17: 4829-36). *In vitro and in vivo* studies have demonstrated that occupancy of the N-terminal pocket of HSP90 by ansamycins and other inhibitors alters HSP90 function and inhibits client protein folding. At high concentrations, ansamycins and other HSP90 inhibitors have been shown to prevent binding of client protein substrates to HSP90 (Scheibel, T., H. *et al.*, 1999, *Proc. Natl. Acad. Sci. U S A* 96:1297-302; Schulte, T. W. *et al.*, 1995, *J. Biol. Chem.* 270:24585-8; Whitesell, L., *et al.*, 1994, *Proc. Natl. Acad. Sci. U S A* 91:8324-8328). Ansamycins have also been demonstrated to inhibit the ATP-dependent release of chaperone-associated protein substrates (Schneider, C., L. *et al.*, 1996, *Proc. Natl. Acad. Sci. U S A*, 93:14536-41; Sepp-Lorenzino *et al.*, 1995, *J. Biol. Chem.* 270:16580-16587), and some of these substrates have been shown to be degraded by a ubiquitin-dependent process in the proteasome (Schneider, C., L., *supra*; Sepp-Lorenzino, L., *et al.*, 1995, *J. Biol. Chem.*, 270:16580-16587; Whitesell, L. *et al.*, 1994, *Proc. Natl. Acad. Sci. USA*, 91: 8324-8328).

This substrate destabilization occurs in tumor and nontransformed cells alike and has been shown to be especially effective on a subset of signaling regulators, *e.g.*, Raf (Schulte, T. W. *et al.*, 1997, *Biochem. Biophys. Res. Commun.* 239:655-9; Schulte, T. W., *et al.*, 1995, *J. Biol. Chem.* 270:24585-8), nuclear steroid receptors (Segnitz, B., and U. Gehring. 1997, *J. Biol. Chem.* 272:18694-18701; Smith, D. F. *et al.*, 1995, *Mol. Cell. Biol.* 15:6804-12), *v-src* (Whitesell, L., *et al.*, 1994, *Proc. Natl. Acad. Sci. U S A* 91:8324-8328) and certain transmembrane tyrosine kinases (Sepp-Lorenzino, L. *et al.*, 1995, *J. Biol. Chem.* 270:16580-16587) such as EGF receptor (EGFR) and Her2/Neu (Hartmann, F., *et al.*, 1997, *Int. J. Cancer* 70:221-9; Miller, P. *et al.*, 1994, *Cancer Res.* 54:2724-2730; Mimnaugh, E. G., *et al.*, 1996, *J. Biol. Chem.* 271:22796-801; Schnur, R. *et al.*, 1995, *J. Med. Chem.* 38:3806-3812). The ansamycin-induced loss of these proteins leads to the selective disruption of certain regulatory pathways and results in growth arrest at specific phases of the cell cycle (Muisse-Heimericks, R. C. *et al.*, 1998, *J. Biol. Chem.* 273:29864-72), and apoptosis of cells so treated (Vasilevskaya, A. *et al.*, 1999, *Cancer Res.*, 59:3935-40).

Growth arrest of this sort, provided it can be made selective, has important ramifications for the treatment of certain proliferative disorders, including cancer. Whereas cancer treatments have thus far been limited to traditional surgical removal, radiation, and/or chemotherapy, and

whereas these procedures have been more or less successful, a need remains to develop additional therapies with increased efficacy and decreased side-effects that can be used alone or in combination with existing therapies. There particularly remains a need for cancer treatments that target specific cancer types. The present invention satisfies these needs and provides related advantages as well.

### Summary of the Invention

Applicants report that many proliferative disorders are associated with aberrant proteins that exhibit a dependence on HSP90. In some cases this dependence manifests as a heightened sensitivity to HSP90 inhibitors such that affected cells can be selectively treated using a dosage that is effective against the aberrant cells but which is ineffective or less effective against normal cells. The aberrant proteins may also exhibit increased proteosome-dependent degradation when in the presence of HSP90 inhibitors. While the invention is not limited by mechanism, increased dependence, sensitivity, and /or disposition to preferential degradation may advantageously be used to treat corresponding proliferative diseases according to the methods of the invention.

Among others, the invention targets two groups of aberrant proteins in particular and the corresponding proliferative disorders they are associated with. Within the first group are fusion proteins generated as a result of non-random chromosomal aberrations (such as translocations, deletions and inversions) that juxtapose parts of the coding sequences of two normal cellular proteins (Rabbitts, T., 1994, *Nature* 372:143-149). Duplication of genetic material within a chromosome resulting in a augmented or semi-duplicative transcripts is also a possibility. Within the second group are mutants and isoforms of cellular proteins that override, dominate, or otherwise obscure the natural gene products and their function. For example, mutants and isoforms of p53 family proteins and other tumor suppressor gene products can act as dominant-negative inhibitors of the corresponding normal protein in heterozygous tumor cells (Blagosklonny, M., *et al*, 1995, *Oncogene*, 11:933-939. Other examples include virally-encoded species of certain kinases, such as v-src and other dominantly-acting mutant oncogene products (Uehara, Y. *et al.*, 1985, *supra*).

Accordingly, in a first aspect the invention features a method of treating a patient having a genetically-defined proliferative disease characterized by a non-random chromosomal aberration. This aberration produces or is capable of producing an oncogenic fusion protein. The method in its broadest embodiment includes (a) providing a



cell, tissue, or fluid sample of a patient suspected of having a genetically-defined proliferative disease; (b) identifying in the cell, tissue, or fluid sample one or more characteristics indicative of the proliferative disease; and (c) administering to the patient a pharmaceutically effective amount of an HSP90-inhibiting compound.

5           The patient may be any organism that can manifest a proliferative disease characterized by an oncogenic fusion protein, which disease is responsive to HSP90 inhibitors. Preferably, but not necessarily, the organism is an animal, more preferably a mammal, and most preferably a human.

10           In preferred embodiments, the inhibitory compound is an ansamycin including but not limited to, *e.g.*, geldanamycin, the geldanamycin derivative, 17-AAG, herbimycin A, and/or macbecin. Most preferably, the ansamycin is 17-AAG. These and other ansamycins and methods of preparing them are well-known in the art. *See, e.g.*, US Patents 3,595,955, 4,261,989, 5,387,584, and 5,932,566. Although preferably the compound is an ansamycin, the method may make use of any compound, synthetic or  
15           nonsynthetic, that can inhibit HSP90. Preferably, the inhibitor binds the ATP-binding site of HSP90, or an HSP90 homolog. Radicol is a nonsynthetic example of a compound useful in the invention described and claimed herein. Libraries of small molecules, synthetic and/or nonsynthetic exist or can be made according to routine, well-known methods and screened for HSP90 binding and/or inhibitory activity. These molecules with  
20           HSP90 binding and/or inhibitory activity are also useful in the methods of the invention.

          In the identifying step of the invention, which is carried out prior to diagnosis where/when there is no previous diagnosis, any technique can be used that can identify or predict a proliferative disorder targetable by HSP90 inhibitors. Especially preferred are antibody-based and nucleic acid hybridization and/or amplification techniques.  
25           Immunoprecipitation, western blotting, and immunoblotting are illustrative examples of antibody-based methods. The antibodies may be monoclonal and/or polyclonal. Illustrative examples of nucleic acid hybridization-based techniques involve Southern blotting, northern blotting, and dot-blotting. Illustrative examples of nucleic acid amplification include standard polymerase chain reactions and variations thereof, *e.g.*,  
30           reverse transcriptase-PCR (RT-PCR). The latter is especially useful for identifying levels of gene expression. Other techniques such as the ligase chain reaction (LCR) are also

well-known and have the ability to distinguish an aberrant gene (and indirectly a protein product produced therefrom) from a normal one, or at least predict genotype and/or phenotype. Other methods of identification include ligand-binding assays and gel-retardation assays that display characteristic binding affinities and/or mobility profiles for normal and variant proteins. Where the fusion protein is also an enzyme, one can establish and/or measure aberrance by enzymatic activity (or lack thereof). Conventional and derivative karyotyping and cytochemical techniques can also be used to identify a proliferative disorder of the invention prior to administration of HSP90-inhibitors. One such method is fluorescent *in situ* hybridization (FISH).

In some embodiments, the proliferative disease is a hematopoietic disorder including but not limited to one selected from the group consisting of T or B cell lymphomas, chronic myeloid leukemias (CMLs), acute promyelocytic leukemias (APLs), acute lymphoid or lymphoblastic leukemias (ALLs), acute myeloid leukemias (AMLs), non-Hodgkin lymphomas (NHLs), and chronic myelomonocytic leukemias (CMMLs). In other embodiments, the disease is characterized by a solid tumor, preferably including but not limited to papillary thyroid carcinoma, Ewing's sarcoma, melanoma, liposarcoma, rhabdomyosarcoma, synovial sarcoma. The embodiments are not necessarily mutually exclusive of one another, and treatment of multiple distinct diseases may simultaneously be effected in a given patient, as the invention has broad-spectrum merit against a variety of different proliferative disorders.

Targeted fusion proteins may contain one or more functional domains or portions thereof, e.g., kinases, DNA binding motifs, etc. Such domains are well-known in the art. Figure 1 illustrates several types of these domains, and the specific fusion proteins, genes, and diseases they can be associated with.

Administration may be by a variety of means. In some preferred embodiments, administration is made *ex vivo*, e.g., removing and treating blood or tissue that is thereafter administered back into the patient. Alternatively, or in combination, administration may be intralésional, e.g., administered to the site of a solid tumor, and/or parenteral. These constitute just some of the many different modes of administration that can be used.

Others are described herein.

In other embodiments, the HSP90-inhibiting compound has an  $IC_{50}$  that is higher (preferably two-fold, more preferably five-fold, and most preferably ten-fold) for cells that do not have characteristics indicative of the proliferative disorder as compared with those cells that do have such characteristics.

5 In other embodiments, the patient may be tested pre- and/or post-administration for sensitivity and or effect of one or more HSP90 inhibitors. This may be done *in vitro* or *in vivo*.

Numerous non-random chromosomal aberrations exist that are associated with proliferative disorders. These include but are not limited to chromosomal translocations, inversions, and deletions. Duplications also account for some aberrant chromosomes and aberrant resulting gene products. All aberrations can be targeted in various aspects of the invention. Illustrative examples of specific aberrations include those listed in Figure 1, which is adapted from Table 1 of Rabbitts, Nature 372:143-149 (1994), and others including but not limited to: inv14 (q11; q32), t(9; 22)(q34; q11), t(1; 19)(q23; p13.3), t(17; 19)(q22; p13), t(15; 17)(q21-q11-22), t(11; 17)(q23; q21.1), t(4; 11)(q21; q23), t(9; 11)(q21; q23), t(11; 19)(q23; p13), t(X; 11)(q13; q23), t(1; 11)(p32; q23), t(6; 11)(q27; q23), t(11; 17)(q23; q21), t(8; 21)(q22; q22), t(3; 21)(q26; q22), 5(16; 21)(p11; q22), t(6; 9)(p23; q34), 9; 9?, t(4; 16)(q26; p13), inv(2; 2)(p13; p11.2-14), inv(16)(p13q22), t(5; 12)(q33; p13), t(2; 5)(2p23; q35), t(9;12)(q34;p13), del(12p), t(9;22),+8,+Ph,i(17q), t(15;17)(q22;q12), t(11;17)(q23;q12), t(16;16)(p13;q22), inv(16)(p13;q22), t(9;11)(p22;q23), t(1;22)(p13;q13), t(3;3)(q21;q26), inv(3)(q21q26), t(3;5)(q21;q31), t(3;5)(q25;q34), t(7;11)(p15;p15), t(8;16)(p11;p13), t(9;12)(q34;p13), t(12;22)(p13;q13), del(5q), del(7q), del(20q), t(11q23), t(12;21)(p13;q22), t(5;12)(q31;p13), t(1;12)(q25;p13), t(12;15)(p13;q25), t(1;12)(q21;p13), t(12;21)(q13;p32), and t(5;7)(q33;q11.2). These are merely a sampling of the many chromosomal aberrations well-known in the art that give rise to particular proliferative disorders treatable according to the invention. For these and others, *see, e.g.*, the National Center for Biotechnology Information (NCBI) databases, including, *e.g.*, the Online Mendelian Inheritance in Man (OMIM) database and related links to nucleotide and protein sequences. For purposes of the present invention, the underlying genetic sequences affected are for the most part known and/or may be deduced using techniques routine in the art.

Targeted in particularly preferred embodiments of the invention are chromosomal aberrations corresponding to t(9; 22)(q34; q11) that give rise to bcr-abl fusion proteins, chronic myelogenous leukemia (CML) and, in some cases, acute lymphoid or lymphoblastic leukemia (for ALL, *see, e.g.*, Erikson et al., *Heterogeneity of chromosome 22 breakpoint in Philadelphia-positive (Ph+) acute lymphocytic leukemia*, Proc. Nat. Acad. Sci. 83: 1807-1811 (1986))).

In a second aspect, the invention features a method of treating cancerous cells in a heterogeneous population of cells. The heterogeneous population includes both cancerous and noncancerous cells, and the cancerous cells are further characterized by fusion proteins that are not produced in the noncancerous cells. The method includes administering to the heterogeneous population a pharmaceutically effective amount of an HSP90-inhibiting compound. The population may be tested by separation of samples from each population into separate subpopulations, cancerous or noncancerous, *e.g.*, where cultured cells of each are tested in parallel for response and/or susceptibility to an HSP90-inhibitor or candidate inhibitor molecule. Alternatively, the population may be mixed, *e.g.*, in an *ex vivo* procedure in which cells of a patient, *e.g.*, blood, are treated and administered back to the patient or to another individual. This method otherwise tracks the various described and/or claimed embodiments and/or combinations of embodiments of the first aspect.

In a third aspect, the invention features a method of treating a patient having a proliferative disease associated with a mutant protein or cellular protein isoform dependent on HSP90, or which disease is otherwise sensitive to HSP90 inhibitors. The method includes (a) providing a cell, tissue, or fluid sample of a patient suspected of having said proliferative disease; (b) identifying in the cell, tissue, or fluid sample one or more characteristics indicative of a mutant or cellular protein isoform; and (c) administering to the patient a pharmaceutically effective amount of an HSP90-inhibiting compound.

In preferred embodiments, the mutant protein or cellular protein isoform is selected from the group consisting of src, RET, p53, p51, p63, and p73. Most preferably selected are isoforms of p53 selected from N239S, C176R, and R213\*, Y236delta, C174Y, M133T, G245D, E258K, 1-293delta, G245C, R248W, E258K, R282W, R175H, R280K,

V143A, R175H, P177S, H178P, H179R, R181P, 238-9delta, G245S, G245D, M246R, R248Q, R249S, R273H, R273C, R273L, and D281Y.

In another preferred embodiment, the proliferative disease to be treated is rheumatoid arthritis.

5 In some embodiments, the mutant protein or cellular protein isoform may give rise to a dominant negative phenotype. In other embodiments, the mutant or cellular protein isoform may give rise to a dominant positive mutant. In either embodiment, the patient may be heterozygous for the normal cellular gene. Other embodiments track those listed for the preceding aspects.

10 In a fourth aspect, the invention features a method of selectively treating cells that express a mutant protein or cellular protein isoform associated with a proliferative disorder and which mutant/isoform is dependent on HSP90, or which disease is otherwise sensitive to HSP90 inhibitors. The method includes (a) providing a population of cells in which at least some of the population express a mutant protein or cellular protein isoform that is  
15 dependent on HSP90 or which are otherwise sensitive to HSP90 inhibitors. The method further includes administering to the population a pharmaceutically effective amount of an HSP90-inhibiting compound. The embodiments for this aspect may otherwise track preceding embodiments.

The foregoing aspects contemplate treatment of existing cell proliferative  
20 disorders. It is expected that the invention may also find use in prophylactic prevention of various proliferative disorders of the invention. Further, and where appropriate, each of the embodiments discussed above and different combinations thereof, including subgenus and sub-Markush groups, may cross-apply to each of the different aspects of the invention. Further, where sequence listings are provided, the invention may in some aspects  
25 contemplate subsequences of the primary sequence listings. Any subsequence within such primary listing is also contemplated for the invention, as well as all allelic variants, and mutant variants and isoforms thereof, as well as corresponding homologs from other organisms and species. Sequences contiguous with and/or in addition to the listed sequences and their above equivalents are also contemplated.

Advantages of the invention include broad-acting treatment or prophylaxis directed to a variety of different proliferative disorders. Other advantages include the efficient and rapid diagnosis and care of patients suffering from proliferative disorders, with minimal apparent adverse effects. Still other advantages, aspects, and embodiments will be  
5 apparent from the figures, the detailed description, and the claims.

### **Brief Description of the Drawings**

Figure 1 illustrates various genetically defined diseases characterized by non-random chromosomal aberrations that give rise to oncogenic fusion proteins. These illustrative aberrations, diseases, and fusion proteins are targeted in various embodiments  
10 of the invention. Other targeted aberrations, diseases, and fusion proteins may be found in the specification and in sources commonly known in the art, e.g., the NCBI and GenBank databases, and journal literature.

### **Detailed Description of the Invention**

#### ***Definitions***

15 As used herein and in the claims the following terms have the following meanings:

A “genetically-defined disease” is one with a basis in DNA. Genetically defined diseases of the invention include “cell proliferative disorders” wherein unwanted cell proliferation of one or more subset(s) of cells in a multicellular organism occurs, resulting in harm, for example, pain or decreased life expectancy to the organism. “Cell proliferative disorders” refer to disorders  
20 wherein unwanted cell proliferation of one or more subset(s) of cells in a multicellular organism occurs, resulting in harm, for example, pain or decreased life expectancy to the organism. Cell proliferative disorders include, but are not limited to, cancers, tumors, benign tumors, blood vessel proliferative disorders, autoimmune disorders and fibrotic disorders. These disorders are not necessarily independent. For example, fibrotic disorders may be related to, or overlap with,  
25 blood vessel disorders, *e.g.*, atherosclerosis (which is characterized herein as a blood vessel disorder that is associated with the abnormal formation of fibrous tissue).

A “non-random chromosomal aberration” is one that occurs with a nonrandom frequency or is selected for in a population of individuals. Chromosomal aberrations of the invention include translocations, *i.e.*, relocation of a fragment of one chromosome onto another

chromosome; inversions, *i.e.*, wherein pieces of a chromosome rotate within the same chromosome, and deletions, *i.e.*, wherein fragments of a chromosome are lost thereby juxtaposing pieces of DNA that previously did not reside immediately beside each other.

5 An “oncogenic fusion protein” is a protein that is non-natural in and of itself but that may contain one or more pieces of other proteins that may or may not naturally occur within a cell. The fusion protein functions by improperly stimulating cell growth, directly or indirectly. In the context of the invention, the term is also associated with a cellular proliferative disease and is preferably encoded by a nucleic acid found in the cell, *e.g.*, as part of a non-random chromosomal aberration. An oncogenic fusion protein may contain domains or portions thereof, *e.g.*, kinases  
10 and/or DNA binding proteins that are well known in the art, or else predicted from their structure to behave as such.

A “fusion” may relate to, as appropriate to a given context, a fusion chromosome, an abnormal mRNA transcribed from the fused portion of the chromosome, or a polypeptide product translated from the abnormal mRNA that is transcribed from the fusion chromosome. These  
15 fusions may result from chromosomal deletions, insertions, and/or translocations. Domains or portions of different genes and gene products are frequently, although not necessarily always, brought together as a consequence of the fusion event. For example, an intragenic deletion can result in an intragenic fusion and give rise to an abnormal protein lacking a component from a second gene. More frequently it occurs that two genes or portions thereof are juxtaposed more or  
20 less, transcribed together as a single transcript, and translated together as a fusion protein bearing contributions from multiple genes or other chromosomal DNA pieces. In such fusions, reading frames can be preserved, *e.g.*, as in preserved functional domains or portions thereof coming from two or more different genes, or else the reading frame can be disrupted, *e.g.*, as in the case of a “missense” or “nonsense” event as these terms are known in the art.

25 By “providing a cell, tissue, or fluid sample of a patient suspected of having said genetically-defined disease” and “identifying one or more characteristics indicative of said disease in or on said cell, tissue, or fluid sample” can mean, although is not limited to the situation where, the sample is withdrawn from the patient in order to perform the analysis or analyses. Many invasive and noninvasive procedures exist, *e.g.*, NMR, ultrasound and other imaging techniques,  
30 that can be used to diagnose, at least in part, an illness and its cause. For example, “tagged” antibodies or other ligands with affinity for a fusion protein or chromosomal aberrancy or

aberrancy product of the invention can be used to make the diagnosis and/or assist in treatment according to methods of the invention.

“Characteristics indicative of said disease” may embrace phenotypes or genotypes and may be measured qualitatively or quantitatively by a variety of techniques. The characteristics  
5 may be observed with the naked eye or else through the assistance of a machine or other diagnostic technique(s). Exemplary techniques of measurement include but are not limited to immunoreactivity and/or precipitation, PCR, LCR, karyotyping, and fluorescence activated cell sorting (“FACS”) as those terms are known and understood in the art.

“Administering” can be by direct means, *e.g.*, intralesional or by parenteral or peripheral  
10 administration to a patient, or else by indirect means, *e.g.*, as by withdrawing a patient’s cells, treating them, and then re-introducing them back into the patient. The latter constitutes an “*ex vivo*” technique.

An “HSP90-inhibiting compound” is one that disrupts the expression, structure, and/or function of an HSP90 chaperone protein and/or a protein that is dependent on HSP90. HSP90  
15 proteins are highly conserved in nature (see, *e.g.*, NCBI accession #'s P07900 and XM 004515 (human  $\alpha$  and  $\beta$  HSP90, respectively), P11499 (mouse), AAB2369 (rat), P46633 (chinese hamster), JC1468 (chicken), AAF69019 (flesh fly), AAC21566 (zebrafish), AAD30275 (salmon), O02075 (pig), NP 015084 (yeast), and CAC29071 (frog). There are thus many different HSP90s, all with anticipated similar effect and similar inhibition capabilities. The HSP90 inhibitor used in  
20 the methods of the invention may be specifically directed against an HSP90 of the specific host patient or may be identified based on reactivity against an HSP90 homolog from a different species, or an artificial HSP90 variant. The inhibitors used may be ring-structured antibiotics, *e.g.*, benzoquinone ansamycins, or other types of molecules, *e.g.*, antisense nucleic acids and molecules such as radicicol.

An “ansamycin” includes but is not limited to geldanamycin, 17-AAG, herbimycin A, and  
25 macbecin. The specific ansamycin 17-AAG stands for 17-allylamino-17-demethoxygeldanamycin. This and other ansamycins that can be used are well-known in the art. *See, e.g.*, U.S. Patent Nos. 3,595,955, 4, 261, 989, 5,387,584, and 5,932,566. Ansamycins may be synthetic, naturally-occurring, or else derivatives of naturally occurring ansamycins that are  
30 prepared using standard chemical derivatization techniques.



A "pharmaceutically effective amount" means an amount which is capable of providing a therapeutic or prophylactic effect. The specific dose of compound administered according to this invention to obtain therapeutic and/or prophylactic effects will, of course, be determined by the particular circumstances surrounding the case, including, for example, the specific compound administered, the route of administration, the condition being treated, the individual being treated, and the tissue or cell type targeted (or not targeted). A typical daily dose (administered in single or divided doses) will contain a dosage level of from about 0.01 mg/kg to about 100 and more preferably 50 mg/kg of body weight of an active compound of this invention. Preferred daily doses generally will be from about 0.05 mg/kg to about 20 mg/kg and ideally from about 0.1 mg/kg to about 10 mg/kg.

A preferred therapeutic effect is the inhibition to some extent of the growth of cells causing or contributing to a cell proliferative disorder. A therapeutic effect will also normally, but need not, relieve to some extent one or more of the symptoms of a cell proliferative disorder other than cell growth or size of cell mass. In reference to the treatment of a cancer, a therapeutic effect refers to one or more of the following: 1) reduction in the number of cancer cells; 2) reduction in tumor size; 3) inhibition (*i.e.*, slowing to some extent, preferably stopping) of cancer cell infiltration into peripheral organs; 3) inhibition (*i.e.*, slowing to some extent, preferably stopping) of tumor metastasis; 4) inhibition, to some extent, of tumor growth; and/or 5) relieving to some extent one or more of the symptoms associated with the disorder.

In reference to the treatment of a cell proliferative disorder other than a cancer, a therapeutic effect refers to either: 1) the inhibition, to some extent, of the growth of cells causing the disorder; 2) the inhibition, to some extent, of the production of factors (*e.g.*, growth factors) causing the disorder; and/or 3) relieving to some extent one or more of the symptoms associated with the disorder.

With respect to viral infections, the preferred therapeutic effect is the inhibition of a viral infection. More preferably, the therapeutic effect is the destruction of cells which contain the virus.

A "cancer" refers to one or more various types of benign or malignant neoplasms. In the case of the latter, these may invade surrounding tissues and may metastasize to different sites, as defined in Stedman's Medical Dictionary 25th edition (Hensyl ed. 1990).

The term "IC<sub>50</sub>" is defined as the concentration of an HSP90 inhibitor required to achieve killing or other growth inhibition of 50% of the cells of a homogenous cell type population, or of a particular cell type, *e.g.*, cancerous versus noncancerous, over a period of time. The IC<sub>50</sub> is preferably, although not necessarily, greater for normal cells than for cells exhibiting a proliferative disorder.

The term "mutant or isoform cellular protein" refers to a variation of a wild-type protein that occurs in a cell and has a particular function. The mutant or isoform cellular protein of the invention preferably associates with or gives rise to a proliferative disorder, *e.g.*, a cancer, whereas the wild-type protein ordinarily does not.

## General

As described and claimed herein, ansamycins and other HSP90 inhibitors can be used to treat two important classes of tumor-promoting (oncogenic) human proteins.

### 1. Oncogenic Fusion Proteins

The first class of target proteins of the invention are fusion proteins generated as a result of non-random chromosomal aberrations (such as translocations, deletions and inversions) that juxtapose parts of the coding sequences of two normal cellular proteins (Rabbitts, T., 1994, *Nature* 372:143-149) leading to the lineage-specific expression of a mutant fusion protein that has biological activities derived from both parent proteins (Barr, F, 1998, *Nat. Genet.* 19:121-124). Without being limiting of the invention, Applicants have discovered that these fusion proteins have a heightened dependence on HSP90 chaperone activity, and/or decreased stability in the presence of HSP90 inhibitors, thus making them selective targets for treatment with HSP90 inhibitors.

#### a. Bcr-abl as an example

One example of heightened HSP90 dependence and inhibitor sensitivity is observed when chronic myelogenous leukemia (CML) cells harboring the fusion oncoprotein p210-bcr-abl are treated with HSP90 inhibitors. This fusion protein is degraded faster and more completely than wild type c-abl protein (An, W *et al*, 2000, *Cell Growth and Differentiation* 11: 355-360). Further experimental evidence that bcr-abl expressing leukemia cells are more sensitive to HSP90 inhibitors than are closely related bcr-abl-negative leukemia lines is found in Honma, Y *et al*,

1995, *Int. J. Cancer* 60:685-688, where it is reported that the IC<sub>50</sub> of herbimycin A in six bcr-abl expressing leukemia cell lines averaged 29.3 nM as compared to a mean IC<sub>50</sub> of 399.3 nM in a panel of four bcr-abl-negative leukemia lines. Illustrative protein and nucleic acid sequences corresponding to embodiments of bcr-abl fusions of the invention include but are not limited to those found in SEQ ID NOs 1-26 and subsequences thereof, which are further discussed below, along with corresponding NCBI accession numbers.

The normal Bcr gene occupies a region of about 135 kb on chromosome 22. It is expressed as mRNAs of 4.5- and 6.7-kb, which apparently encode for the same cytoplasmic 160-kD protein, and contains 23 exons as well as an unusual inverted repeat flanking the first exon. The BCR protein reportedly contains a unique serine/threonine kinase activity and at least two SH2 binding sites encoded in its first exon and a C-terminal domain that functions as a GTPase activating protein for p21(rac) (Diekmann et al., *Nature* 351: 400-402 (1991). Chisoe et al., *Genomics* 27: 67-82 (1995), sequenced the complete BCR gene and greater than 80% of the human ABL gene, which are both involved in the t(9;22) translocation (Philadelphia chromosome) associated with more than 90% of chronic myelogenous leukemia, 25 to 30% of adult and 2 to 10% of childhood acute lymphoblastic leukemia, and rare cases of acute myelogenous leukemia. Comparison of the gene with its cDNA sequence revealed the positions of 23 BCR exons and putative alternative BCR first and second exons. From the sequence of four newly studied Philadelphia chromosome translocations and a review of several other previously sequenced breakpoints, Chisoe et al. found a variety of breakpoints and recombinations sites possible within the genes. Thus, despite the normal chromosomes and genes each being known (9 and 12; bcr and abl), and the fact that combinations of these genes are known to lead to forms of CML and ALL, the precise genetic breakpoint/recombination junctions that lead to these diseases can vary.

This heterogeneity likely also applies to some non bcr-abl chromosomal aberrations of the invention as well. Nevertheless, because the genes and/or chromosomes involved are known to have a part in the disorders, the disorders are said to be "genetically defined."

## b. Other oncogenic fusion proteins

Oncogenic fusion proteins in general are thought to be inherently unstable. To the extent these unstable oncogenic fusion proteins make use of HSP90, they are susceptible of the methods claimed herein. Because the fusion genes and their protein products exert overtly oncogenic activity (Deininger, M *et al*, 2000, *Cancer Res.* 60:2049-2055), preferential degradation of these labile proteins induced by HSP90 inhibitors will have therapeutic value in diseases where the fusion protein is expressed. The present invention thus includes treatment of patients with tumors that are dependent upon other oncogenic fusion proteins that arise from non-random genetic aberrations. An illustrative but nonexhaustive list of these tumors is included in Figure 1, adapted from Table 1 of Rabbitts, T., 1994, *Nature* 372:143-149. The list may be supplemented by additional information found, *e.g.*, in Rowley, J, 1999, *Semin. Hematol.* 36:59-72 and other publications known in the art, as well as discussion below.

Myeloid cancers in particular are within the scope of the invention and include chromosomal abnormalities that give rise to oncogenic fusion proteins that drive the growth of chronic myeloid leukemia (CML), chronic myelomonocytic leukemia (CMML), acute myeloid leukemia (AML), acute promyelocytic leukemia (APL), and acute lymphoblastic leukemia (ALL). The following chromosomal aberrancies give rise to some illustrative fusions implicated in various forms of ALL:

t(1:19)(q23:p13) Pro-pre-B acute lymphoblastic leukemia

t(12:21)(p13;q32) Pro-pre-B acute lymphoblastic leukemia

t(9:22)(q34;q11) B or B-myeloid acute lymphoblastic leukemia

t(9:12)(q34:p13) Acute B-lymphoblastic leukemia

del(12p) Acute B-lymphoblastic leukemia

Specific genes and proteins thereof implicated in various ALL forms include the *MLL* gene and the *TEL* gene, which are commonly rearranged in tumors. Rowley, J, *supra*. Each has numerous fusion partners. ETV6 denotes the name of the TEL gene product. Fusion of TEL/ETV6 to an acyl CoA synthetase, ACS2, results from a t(5;12)(q31;p13) AML event (Yagasaki, F *et al*, 1999, *Genes Chromosomes Cancer* 26:192-202); fusion of TEL/ETV6 to ABL-related gene (ARG)

results from a t(1;12)(q25;p13) AML event (Iijima, Y *et al*, 2000, *Blood* 95:2126-2131); fusion of TEL/ETV6 to the neurotrophin-3 receptor TRKC results from a t(12;15)(p13;q25) AML event and gives rise to congenital fibrosarcoma (Liu, Q *et al*, 2000, *EMBO J.* 19:1827-1838, Eguchi, M *et al*, 1999, *Blood* 93:1355-1363); fusion of TEL/ETV6 to the aryl hydrocarbon receptor ARNT results from a t(1;12)(q21;p13) event and gives rise to acute myeloblastic leukemia (AML-M2) (Salomon-Nguyen, F *et al*, 2000, *Proc. Natl. Acad. Sci.* 97:6757-6762); and fusion of TEL/ETV6 to AML-1, the DNA-binding subunit of the AML-1/CBF $\beta$  transcription factor results from a (12;21)(q13;p32) event that can give rise to acute lymphoblastic leukemia (ALL, Shurtleff, SA *et al*, 1995, *Leukemia* 9:1985-1989) and, in some cases, non-Hodgkin's lymphoma (NHL).

Another illustrative fusion within the scope of the invention is the EWS/FLI-1 hybrid protein that is the hallmark of Ewing's sarcoma and the primitive neuroectodermal tumor family (Silvany, *et al*, 2000, *Oncogene* 19:4523-4530).

Yet another illustrative family of fusion proteins within the scope of the invention is the group of fusion proteins arising from chromosomal rearrangements involving the *RET* gene in thyroid cancer (Kolibaba, K, *et al*, 1997, *Biochem. Biophys. Acta* 1333:F217-F248). Rearrangements of *RET*, resulting in juxtaposition of the RET tyrosine kinase domain with one of three 5' sequences (RET-PTC-1, -2 and -3) generate fusion proteins comprising the kinase domain of RET fused to parts of the genes *H4* (RET-PTC-1), *R1a* of cAMP-dependent protein kinase A (RET-PTC-2) and ELE-1 (RET-PTC-3).

The scope of the present invention also includes cancers and other proliferative diseases, e.g., rheumatoid arthritis, now known or discovered in the future to be characterized by specific chromosomal aberrations giving rise to fusion proteins.

In at least some cases, heterogeneity of breakpoints within the affected chromosomes is possible, thus providing for the possibility of many different DNA fusions and amino acid sequence variations than those specifically listed in the SEQ ID NOs provided, and which can also be formed by the chromosomal rearrangements, e.g., translocations, inversions, deletions, insertion/duplications, etc., so designated. For example, many different abl-bcr gene combinations and corresponding fusion proteins can be designated by the t(9;22)(q34;q11) translocation event, and all—not just those listed below—are included within the purview of the designation, t(9;22)(q34;q11).

Aberrant proteins of the invention, at least in some instances, feature one or more properties of the individual normal parent genes' gene products (normal polypeptide gene product(s), including e.g., functional and structural domains and subportions thereof resulting from transcription and translation of normal parent genes on normal  
5 chromosomes) but otherwise lack exact identity and function with the parent genes' protein products. Chromosomal aberrations may give rise to in-frame fusions or frame-shifts, the latter of which can account for missense or nonsense translation of at least a portion of the mRNA, and thereby result in aberrant polypeptide product(s).

Of the SEQ ID NOs discussed herein, some reflect fusion genes, some reflect  
10 fusion gene products, e.g., mRNAs and peptides, and some reflect portions of such entities. Still some others reflect recombination "hot spots" in the normal genes that have a general propensity to form a chromosomal aberration. Each of the above sequences may be useful as diagnostic markers in appropriate embodiments of the invention and/or may be characteristic of a given proliferative disorder (or patient exhibiting such and,  
15 accordingly, a candidate for treatment according to some methods of the invention.

While the specific sequences discussed are predominantly human in origin, it is understood that other animal "homologs" of the corresponding human sequences are known in the art and are intended to be within the purview of various aspects of the invention. Because HSP90s are also found in plants, plants and plant cells and tissues  
20 exhibiting fusion protein products that give rise to undesirable traits may also be treatable in some aspects and embodiments of the invention. The NCBI nucleotide and protein databases are an example of where such sequences can be found. It is also appreciated that the complete human genome and other genomes have been sequenced, and continue to be sequenced at a high rate, thus facilitating the identity of sequences contiguous with  
25 those listed herein and homologs thereto.

Further, some of the sequences listed herein may contain errors associated with the logistical complexities of compiling such extensive data, and the true sequences should be interpreted to be within the scope of the invention, either literally or under the doctrine of equivalents, as they are known in the art.

30 As those of ordinary skill will appreciate, allelic variations and different isotype proteins are also possible for some genes, e.g., the product of differential splicing events in

mRNA, and these are likewise considered within the scope of the invention. Further, some of the NCBI and SEQ ID NOs listed below are for wild-type genes, and are included to give an indication of the different chimeric possibilities for the fused counterpart during a chromosomal aberration according to the invention. Should any of the sequences listed below be in error, such should be construed consistent with what is commonly understood in the art—irrespective of how presented in the application.

**c. Further Discussion of Illustrative Chromosomal Aberrancies**

*Convention: where two or more SEQ ID NOs are provided per NCBI accession #, peptide(s) shall be listed first where applicable, followed by corresponding mRNA/cDNA and/or genomic sequence as the case may be. The terms “nucleotide” and “nucleotides” are interchangeable with, and may be symbolized by, “nt.”*

**t(9; 22)(q34; q11)**

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # S72478, corresponding to SEQ ID NOs 1 and 2, illustrates one aberrant polypeptide/mRNA in a patient having CML and another patient having ALL. The junction for the nucleic acid sequence between the BCR and ABL genes is stated to reside between nucleotides 100 and 101., with 1-100 derived from BCR and 101-140 derived from ABL.

NCBI #M19695 (SEQ ID NO 3) illustrates a nucleic acid sequence identified from a human myelocytic chimeric bcr/chromosome 9 fusion (CML K562 cell line).

NCBI #M30829 (SEQ ID NOs 4 and 5) illustrates a partial bcr/abl fusion protein mRNA.

NCBI #M13096 (SEQ ID NO 6) illustrates a human chimeric bcr/c-abl fusion protein gene characteristic of cell line K562.

NCBI #M30832 (SEQ ID NOs 7 and 8) corresponds to a human bcr/abl fusion protein, partial cds, clone E3 from cell line EM2.

NCBI # AJ131466 (SEQ ID NOs 9 and 10) corresponds to a partial human bcr/abl (major breakpoint) fusion peptide and the underlying nucleic acid encoding it. Nucleotides 1-373 are said to derive from exons 11-14 of the bcr gene, and nucleotides 374-997 are said to derive from exons 2-4 of the abl gene.

5 NCBI # AF192533 (SEQ ID NOs 11 and 12) corresponds to a partial human bcr/abl (major breakpoint) fusion mRNA. Nucleotides 1-289 are said to come from the bcr gene of chromosome 22 and nucleotides 290-305 from the abl gene of chromosome 9.

10 NCBI # AF321981 (SEQ ID NO 13) corresponds to a BCR-ABL fusion transcript e15a2 mRNA sequence. This particular fusion is stated to result from results from a translocation between the 3' portion of the c-ABL oncogene on chromosome 9 and exon 15 of the BCR gene on chromosome 22; t(9;22).

15 NCBI # M17543 (SEQ ID NO 14) corresponds to at least a portion of a Philadelphia chromosome breakpoint cluster region associated with one embodiment of a bcr abl fusion gene. Nucleotides 1-31 are said to be exon 1 and nucleotides 32-63 are said to be intron A.

NCBI # M17542 (SEQ ID NOs 15 and 16) corresponds to a human bcr/abl fusion protein mRNA (product of translocation t(22q11; 9q34)), exons 1 and 2. Nucleotides 1-31 are stated to denote exon 1 and nucleotides 32-63 are stated to denote exon 2.

20 NCBI # M17541 (SEQ ID NOs 17 and 18) corresponds to a human bcr/abl fusion protein mRNA (product of translocation t(22q11; 9q34)), exons 1 and 2. Nucleotides 1-31 are stated to denote exon 1 and nucleotides 32-63 are stated to denote exon 2.

25 NCBI # AB069693 (SEQ ID NOs 19 and 20) denotes a human partial mRNA corresponding to a bcr/abl e8a2 fusion protein. BCR exons 7 (nucleotides 1-53) and 8 (nucleotides 54-194) are joined to ABL intron 1b inverted (nucleotides 195-249) and ABL exon a2 (nucleotides 250-423).

NCBI # AJ131467 (SEQ ID NOs 21 and 22) correspond to a human partial BCR/ABL chimeric fusion peptide and corresponding mRNA. Nucleotides 1-117 denote exon 1 of the bcr gene, nucleotides 118-193 and 194-298 denote exons 12 and 13 of the



bcr gene, and nucleotides 299-472, 473-768, and 769-922 respectively denote exons 2-4 of the abl gene.

NCBI # AF113911 (SEQ ID NOs 23 and 24) correspond to a partial BCR-ABL minor breakpoint peptide (BCR-ABL fusion) mRNA. Nucleotides 1-455 are stated to be  
5 from chromosome 22 and nucleotides 456-1079 from chromosome 9.

NCBI # AF251769 (SEQ ID NOs 25 and 26) correspond to a human partial bcr/abl e1-a3 chimeric fusion protein (BCR/ABL e1-a3) mRNA. Nucleotides 1-455 are stated to be from chromosome 22 and nucleotides 456-1079 from chromosome 9.

#### **inv14 (q11; q32)**

10 This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # X82240 (SEQ ID NOs 27 and 28) correspond to at least a portion of an mRNA for the gene TCL1, which is disrupted in aberrations of the type noted.

NCBI # NM\_021966 (SEQ ID NOs 29 and 30) relate to a human T-cell  
15 leukemia/lymphoma 1A (TCL1A), mRNA.

NCBI # X82241 (SEQ ID NO 31) relates to a 5' portion of a human TCL1 gene. Nucleotides 496-560 are said to correspond to exon 1.

NCBI # M14198 (SEQ ID NOs 32 and 33) relate to a human chromosome 14 paracentric inversion producing an heavy chain/T-cell receptor J-alpha fusion protein.

20 NCBI # X03752 (SEQ ID NOs 34 and 35) relate to a human gene for rearranged Ig V(H) are said to encode the IgVH region (108 aa) and nucleotides 324 to 377 are said to encode 18 amino acids of the TCR-J-alpha protein.

NCBI # M12071 (SEQ ID NOs 36 and 37) relates to a human Ig heavy-chain V-region gene (VII family) rearranged to T-cell receptor alpha-chain D-J-sp region (IgT) in  
25 an inv(14)(q11; q32), SUP-T1 cell line. Nucleotides 121-166 are said to derive from exon 1 of the IgH gene, nucleotides 167-248 from intron 1 of the IgH gene, nucleotides 249-623 from exon 2 of the IgH gene, and nucleotides 624-675 from intron 2 of the IgH gene.

NCBI # S45947 (SEQ ID NOs 38 and 39) relate to an IgT=T cell specific exon ET-immunoglobulin VH-T cell receptor J alpha fusion [human, T cell lymphoma cell line SUP-T1, mRNA Mutant, 508 nt]. Nucleotides 34-507 are stated to be IgT coding sequence.

5 NCBI # S45207 (SEQ ID NOs 40 and 41) relate to an IgT=T cell specific exon ET-exon EX-immunoglobulin VH-T cell receptor J alpha fusion [human, T cell lymphoma cell line SUP-T1, mRNA Mutant, 616 nt]. Nucleotides 130-616 are stated to be IgT coding sequence.

**t(1; 19)(q23; p13.3)**

10 This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # M31522 (SEQ ID NOs 42 and 43) relate to a human translocation (t1;19) fusion protein (E2A/PRL) mRNA, 3' end. ]. Nucleotides 1-1653 are stated to encode a portion of an E2A/PRL fusion protein.

15 **t(17; 19)(q22; p13)**

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # M95586 (SEQ ID NOs 44 and 45) relate to a human E2A/HLA fusion protein (E2A/HLF) mRNA, complete cds. Nucleotides 31-1755 are said to be coding  
20 sequence.

**t(15; 17)(q21-q11-22)**

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # S50916 (SEQ ID NOs 46 and 47) relate to a PML-RAR fusion gene  
25 {fusion transcript} [human, mRNA Partial, 1284 nt]. . Nucleotides 1-1251 are said to be coding sequence.

NCBI # M73779 (SEQ ID NOs 48 and 49) relate to a human PML-RAR protein (PML-RAR) mRNA, complete cds; coding sequence: nucleotides 67-2460.

NCBI # AJ417079 (SEQ ID NOs 50 and 51) relate to a human partial mRNA for PML/RARA fusion protein (PML/RARA gene); Nucleotides 1-109 derive from exon 6 of PML, nucleotides 110-172 from intron 2 of RARA, and nucleotides 173-296 from exon 3 of RARA.

### **t(11; 17)(q23; q21.1)**

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # AAB29813 (SEQ ID NO 52) relates to a retinoic acid receptor alpha, RAR alpha(PLZF=zinc finger protein, PLZF-RAR alpha isoform A=fusion protein) {translocation} [human, acute promyelocytic leukemia patient, Peptide Mutant, 858 aa].

NCBI # AAB29814 (SEQ ID NO 53) relates to a PLZF=zinc finger protein(retinoic acid receptor alpha, RAR alpha, RAR alpha 1-PLZF isoform B=fusion protein) {translocation} [human, acute promyelocytic leukemia patient, Peptide Mutant, 277 aa].

### **t(4; 11)(q21; q23)**

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # L22179 (SEQ ID NOs 54 and 55) relate to a human MLL-AF4 der(11) fusion protein mRNA, complete cds. Nucleotides 5-6940 are said to be coding sequence.

NCBI # S67825 (SEQ ID NOs 56 and 57) relate to a human ALL1-AF4 fusion protein mRNA, partial cds. Nucleotides 1-585 are said to derive from chromosome 11 and nucleotides 586-832 from chromosome 4.

NCBI # AF024541 (SEQ ID NOs 58 and 59) relate to a human MLL-AF4 fusion protein mRNA, partial cds. The codons are said to start with nucleotide 3.

NCBI # AF031404 (SEQ ID NOs 60 and 61) relate to a human MLL-AF4 fusion protein mRNA, partial cds. Nucleotides 1-305 are said to derive from chromosome 11 and nucleotides 306-741 from chromosome 4. Codons begin with nucleotide 3.

5 NCBI # L04731 (SEQ ID NO 63) relates to a human translocation T(4;11) of the human ALL-1 gene to chromosome 4.

NCBI # AF177237 (SEQ ID NOs 64 and 65) relate to human cell-line MV4-11, MLL/AF4 fusion protein (MLL/AF4) mRNA, partial cds. Nucleotides 1-62 derive from exon 6 of the MLL gene on chromosome 11, and nucleotides 63-450 from exon 5 of the AF4 gene on chromosome 4.

10 NCBI # AF177236 (SEQ ID NOs 66 and 67) relate to a human A1 MLL/AF4 fusion protein (MLL/AF4) mRNA, partial cds. Nucleotides 1-63 are stated to derive from exon 6 of the MLL gene on chromosome 11, and nucleotides 64-450 from exon 5 of the AF4 gene on chromosome 4.

15 NCBI # AF031403 (SEQ ID NO 68) relates to a human MLL/AF4 translocation breakpoint t(4;11)(q21;23). Nucleotides 1-105 are said to derive from exon 5 of MLL, nucleotides 435-508 from exon 6 of MLL, nucleotides 2195-2326 from exon 7 of MLL, nucleotides 2874-2987 from exon 8 of MLL, and nucleotides 3645-6983 from AF4.

20 NCBI # AF177238 (SEQ ID NOs 69 and 70) relate to a human A1 AF4-MLL fusion protein (AF4-MLL) mRNA, partial cds. Nucleotides 1-484 are said to derive from exon 3 of AF4 and nucleotides 485-596 from exon 7 of MLL.

NCBI # AF177239 (SEQ ID NOs 71 and 72) relate to a human cell-line MV4-11 AF4-MLL fusion protein (AF4-MLL) mRNA, partial cds. Nucleotides 1-484 are said to derive from exon 3 of AF4 and nucleotides 485-596 from exon 7 of MLL

25 NCBI # AF397907 (SEQ ID NO 73) relates to a human AF4/MLL translocation breakpoint region. Nucleotides 1-437 are said to derive from intron 3 of AF6, nucleotides 440-631 from intron 6 of MLL, and nucleotides 632-747 from exon 7 of MLL. The breakpoint is approximately nucleotide 438-439, which was undetermined due to GC compressions.

NCBI # AF024543 (SEQ ID NO 74) relates to a human MLL/AF4 translocation breakpoint t(4;11)(q21;q23).

**t(9; 11)(q21; q23)**

5 This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # S82034 (SEQ ID NO 75) relates to an MLL-AF9=fusion gene {fusion site} [human, peripheral blood, acute myeloid leukemia FAB type M1 patient UPN 427, mRNA Partial, 60 nt].

**t(11; 19)(q23; p13)**

10 This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # S81007 (SEQ ID NO 76) relates to an MLL/ENL=fusion gene {rearranged derivative 11 junction region} [human, leukemic lymphoblasts, T-cell acute lymphoblastic leukemia patient RUPN2, Genomic Mutant, 74 nt]. The authors indicated that the first 34  
15 nt derived from MLL intron 8 on 11q23, and nt 35-74 from the ENL-distal region on 19p13.3

NCBI # S81008 (SEQ ID NO 77) relates to an ENL {rearranged derivative 19 junction region} [human, leukemic lymphoblasts, T-cell acute lymphoblastic leukemia patient RUPN2, Genomic Mutant, 84 nt]. The authors indicated that nt 55-84 derived  
20 from MLL gene 3' region on 11q23.

**t(X; 11)(q13; q23)**

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # NM\_005938 (SEQ ID NOs 78 and 79) relate to a human  
25 myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, Drosophila); translocated to, 7 (MLLT7), mRNA. Nucleotides 183-1688 denote an MLLT7 coding

region, with nucleotides 465-719 and 480-749 corresponding to a forkhead and forkhead domain, and G and C allelic variations possible at nucleotide 1435.

NCBI # X93996 (SEQ ID NOs 80 and 81) relate to a human mRNA for AFX protein. Nucleotides 183-1688 are said to be AFX coding sequence.

5 **t(1; 11)(p32; q23)**

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # AF331760 (SEQ ID NO 82) relates to human clone UPN5379L mRNA sequence (bone marrow acute lymphoblastic FAB L2 type).

10 **t(6; 11)(q27; q23)**

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # S82519 (SEQ ID NOs 83 and 84) relate to a human MLL-AF6 fusion protein mRNA, partial cds, identified in a leukemic patient, and with the breakpoint stated  
15 to be approximately between nt 26 and 27.

NCBI # S82521 (SEQ ID NOs 85 and 86) relate to a an MLL-AF6=fusion gene {breakpoint region, clone b} [human, blood, leukemic patient 2, mRNA Partial, 69 nt]. The breakpoint here is said to reside between nt 24 and 25.

NCBI # S82517 (SEQ ID NOs 87 and 88) relate to an MLL-AF6=fusion gene  
20 {breakpoint region} [human, blood, leukemia patient 1, mRNA Partial, 69 nt]. The breakpoint here is said to reside between nt 24 and 25.

**t(11; 17)(q23; q21)**

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

25 NCBI # S72604 (SEQ ID NOs 89 and 90) relate to an AF17...ALL-1 {reciprocal translocation} [human, acute myeloid leukemia patient, mRNA Partial Mutant, 3 genes,

228 nt]. Nucleotides 1-88 are said to derive from AF17 and nucleotides 89-228 from ALL-1.

NCBI # (SEQ ID NOs 91 and 92) relate to a human myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, *Drosophila*); translocated to, 6 (MLLT6), mRNA.

5 Nucleotides approximating 22-168 are said to encode a PHD zinc finger motif and nucleotides 2185-2292 (amino acids 729-764) are said to encode a leucine zipper motif, with A and G allelic variations at nt 592 possible.

#### **t(8; 21)(q22; q22)**

10 This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # (SEQ ID NOs 93 and 94) relate to a human mRNA for AML1-MTG8 fusion protein, complete cds. The coding sequence is said to be nucleotides 1579-3837 and the breakpoint is said to be between nt 2110 and 2111.

15 NCBI # S78158 (SEQ ID NOs 95 and 96) relate to a human AML1-ETO fusion protein (AML1-ETO) mRNA, partial cds. Nucleotides 1-1767 are said to denote the coding sequence.

NCBI # S78159 (SEQ ID NOs 97 and 98) relate to a human AML1-ETO fusion protein (AML1-ETO) mRNA, partial cds. . Nucleotides 1-696 are said to denote the coding sequence and nucleotides 40 and 41 are said to represent the junction point.

20 NCBI # D14822 (SEQ ID NOs 99 and 100) relate to a human chimeric partial mRNA derived from AML1 and MTG8(ETO) gene sequences. Nucleotides 1-101 are said to derive from the AML1 gene on chromosome 21 and nucleotides 102-799 from the MTG8 (ETO) gene on chromosome 8.

25 NCBI # S45790 (SEQ ID NO 101) relates to a AML1/ETO=acute myelogenous leukemia {translocation breakpoint} [human, Genomic Mutant, 237 nt].

NCBI # Z35296 (SEQ ID NO 102) relates to a human AML1/ETO alternative fusion transcript mRNA, 276bp. Nucleotides 1-117 are said to derive from AML1 and 186-276 are said to derive from ETO.

NCBI # D14823 (SEQ ID NOs 103 and 104) relate to a human chimeric mRNA derived from AML1 gene and MTG8(ETO) gene, partial sequence. Nucleotides 1-101 are said to be derived from the AML1 gene on chromosome 21 and nucleotides 102-1446 are said to be derived from the MTG8(ETO) gene on chromosome 8, with the coding  
 5 sequence denoted nt 1-757.

**t(3; 21)(q26; q22)**

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # S69002 (SEQ ID NOs 105 and 106) relate to a AML1-EVI-1=AML1-  
 10 EVI-1 fusion protein {rearranged translocation} [human, leukemic cell line SKH1, mRNA Mutant, 5938 nt]. The author indicated the boundary between AML1 and EVI-1 to be between nt 2138 and 2139, with the coding sequence being 1603-5790.

NCBI # L21756 (SEQ ID NOs 107 and 108) relate to a human acute myeloid leukemia associated protein (AML1/EAP) mRNA, complete cds. Nucleotides 1-786 are  
 15 said to denote the coding sequence.

NCBI # S76343 (SEQ ID NO 109) relates to AML1...EAP {translocation breakpoint} [human, chronic myelogenous leukemia in blast crisis patient, Genomic Mutant, 3 genes, 470 nt]. Nucleotides 1-125 are said to derive from AML1 and nucleotides 126-470 are said to derive from EAP.

**20 t(16; 21)(p11; q22)**

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # S71718 (SEQ ID NOs 110 and 111) relate to a TLS/FUS...ERG {translocation} [human, myeloid leukemia patient, peripheral blood, bone marrow cells,  
 25 mRNA Partial Mutant, 3 genes, 55 nt]. Nucleotides 46-55 are said to derive from ERG, with the codon start beginning with nt 3.

NCBI # S71805 (SEQ ID NOs 112 and 113) relate to a TLS/FUS...ERG {translocation} [human, myeloid leukemia patient, peripheral blood, bone marrow cells,



mRNA Partial Mutant, 3 genes, 99 nt]. Nucleotides 1-89 are said to derive from TLS/FUS and nucleotides 90-99 from ERG, with the codon start beginning with nt 3.

NCBI # Y10001 (SEQ ID NO 114) relates to a DNA fragment containing fusion point of FUS gene and ERG gene, translocation t(16;21)(p11;q22).

5 **t(6; 9)(p23; q34)**

NCBI # X64229 (SEQ ID NOs 115 and 116) relate to a human dek mRNA. The coding sequence is said to be nt 34-1161.

**inv(9;9)**

10 This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # X63689 (SEQ ID NO 117) relates to a human translocation breakpoint in the "can" gene sequence. The translocation breakpoint is said to be 174..175.

NCBI # M93651 (SEQ ID NOs 118 and 119) relate to a human set gene, complete cds. The coding sequence is said to be 4-837.

15 **t(4; 16)(q26; p13)**

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

20 NCBI # Z14955 (SEQ ID NOs 120 and 121) relate to a human mRNA encoding the interleukin 2/BCM fusion protein. Nucleotides 1-321 derive from exons 1-3 of IL-2 and nucleotides 322-864 from the BCM gene.

**inv(16)(p13q22)**

This inversion is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

25 NCBI # AF251768 (SEQ ID NOs 122 and 123) relate to a human PCBFB/MYH11E chimeric fusion protein (CBFB/MYH11) mRNA, partial cds.

Nucleotides 1-41 correspond to exon 5 of CBFB and nucleotides 42-78 to exon 7 of MYH11.

NCBI # AF249898 (SEQ ID NOs 124 and 125) relate to a human PCBFbeta/MYH11A chimeric fusion protein (CBFbeta/MYH11A) mRNA, partial cds.

5 Nucleotides 1-41 correspond to exon 5 of CBFB and nucleotides 42-102 to exon 12 of MYH11.

NCBI # AF249897 (SEQ ID NOs 126 and 127) relate a human PCBFb-MYH11d chimeric fusion protein (CBFB/MYH11D) mRNA, partial cds. Nucleotides 1-41 correspond to exon 5 of CBFB and nucleotides 42-109 to exon 8 of MYH11.

10 NCBI # AF390860 (SEQ ID NO 128) relates to a human isolate UPN2 CBFB/MYH11 translocation breakpoint region sequence.

NCBI # AF390859 (SEQ ID NO 129) relates to a human isolate UPN1 CBFB/MYH11 translocation breakpoint region sequence.

15 NCBI # AF202996 (SEQ ID NOs 130 and 131) relate to human core binding factor beta-smooth muscle myosin heavy chain fusion protein (CBFB-MYH11) mRNA, partial cds. Nucleotides 1-46 are said to correspond to 16q22 and nucleotides 47-89 to 16p13. Nucleotide 50 is said to be a "t" in some cases.

### **t(5; 12)(q33; p13)**

20 This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # NM\_001987 (SEQ ID NOs 132 and 133) relate to a human ets variant gene 6 (TEL oncogene) (ETV6), mRNA. Nucleotides 25-1383 are said to correspond to coding sequence, of which nt 136-393 are said to correspond to a sterile alpha motif (SAM) pointed domain, nt 1036-1290 to an erythroblast transformation-specific (Ets)-  
25 domain, and wherein allelic variations including "c"s and "t"s at each of nt 798, nt 1541, and nt 1598, and an "a"s and "c"s at each of nt 1822 and 1881.

NCBI # U11732 (SEQ ID NOs 134 and 135) relate to a human ets-like gene (tel) mRNA, complete cds. The coding sequence is said to be from nt 25-1383, and the translocation breakpoint said to occur after nt 487.

**t(2; 5)(2p23; q35)**

5 This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI #14: AF032882 (SEQ ID NO 136) relates to a human anaplastic lymphoma kinase receptor (ALK) and nucleophosmin (NPM) truncated genes at a t(2;5) translocation breakpoint. Nucleotides 1-46 are said to be ALK sequence that is truncated at 3' due to  
10 translocation, and nucleotides 1370-1451 are said to be NPM sequence that is truncated at 5' due to translocation.

NCBI # S82740 (SEQ ID NO 137) relates to a NPM/ALK=fusion gene {translocation breakpoint} [human, lymphoma cells SUP-M2, Genomic, 1565 nt].

NCBI # S82725 (SEQ ID NO 138) relates to a NPM/ALK=fusion gene  
15 {translocation breakpoint} [human, lymphoma cells SU-DHL-1, Genomic, 1679 nt].

NCBI # U04946 SEQ ID NOs 139 and 140) relate to a human nucleophosmin-anaplastic lymphoma kinase fusion protein (NPM/ALK) mRNA, complete cds. The recombination junction is said to occur at nt 353.

**t(11; 22) (q24; q12)**

20 This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # AJ229320 (SEQ ID NO 141) relates to a human translocation t(11;22) DNA in ewings's tumor derivative 22 (isolate: EWTUM64/ MIC). Nucleotides 1-88 are said to denote EWS sequence and nucleotides 89-180 FLI-1 sequence.

25 NCBI # AJ229311 SEQ ID NO 142) relates to a human translocation t(11;22) DNA in ewings's tumor derivative 22 (isolate: EWTUM56/ EW20). Nucleotides 1-114 are said to denote EWS sequence and nucleotides 115-180 FLI-1 sequence.

NCBI # AF177752 (SEQ NO 143) relates to a human clone Jugo Ewing's sarcoma-specific EWS-FLI1 chimera target sequence.

NCBI # AF177751 (SEQ ID NO 144) relates to a human Juyon Ewing's sarcoma-specific EWS-FLI1 chimera target sequence.

5 NCBI # AF177750 (SEQ ID NO 145) relates to a human clone Iti Ewing's sarcoma-specific EWS-FLI1 chimera target sequence.

NCBI # AF327066 SEQ ID NOs 146 and 147) relate to a human Ewings sarcoma EWS-Fli1 (type 1) oncogene mRNA, complete cds.

10 NCBI # XM\_060745 (SEQ ID NOs 148 and 149) relate to a human similar to EWS/FLI1 activated transcript 2 (H. sapiens) (LOC127935), mRNA. Nucleotides 10-225 and 13-195 are said to denote src homology 2 (SH2) domains.

NCBI # AF403479 SEQ ID NOs 150 and 151) relate to a human EWS/FLI1 activated transcript 2 protein mRNA, complete cds.

15 NCBI # AF020264 (SEQ ID NOs 152 and 153) relate to a human EWS/FLI1 activated transcript 2 homolog (EAT-2) gene, partial cds.

NCBI # AF020263 (SEQ ID NOs 154 and 155) relate to a Mus musculus EWS/FLI1 activated transcript 2 (EAT-2) mRNA, complete cds.

20 NCBI # S72620 SEQ ID NOs 156 and 157) relate to a EWS...Fli1 [human, T93-113 tumor, mRNA Partial Mutant, 3 genes, 229 nt]. Nucleotides 1-85 are said to denote partial EWS gene sequence and nt 86-229 are said to denote partial FLI-1 sequence.

NCBI # S64709 (SEQ ID NO 158) relates to EWS...Fli-1 {translocation} [human, IARC-EW11 Ewing's tumor-derived cells, mRNA Mutant, 3 genes, 100 nt]. Nucleotides 1-18 are said to denote partial EWS gene sequence and nt 19-100 are said to denote partial FLI-1 sequence.

25 NCBI # S62665 (SEQ ID NOs 159 and 160) relate to a type 4 EWS-FLI1 fusion {translocation} [human, primitive neuroectodermal tumor cell line TC-32, mRNA Partial Mutant, 60 nt]. Positions 1-31 are said to be from the 5' portion of EWS on chromosome

22 and positions 32-60 are said to be from the 3' (DNA-binding) region of FLI1 on chromosome 11.

### **inv(10)(q11.2; q21)**

This aberration is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # AF395885 (SEQ ID NO 161) relates to a human H4/RET fusion mRNA, partial sequence. tyrosine kinase domain of the ret. Nt 1-83 are said to derive from H4, nt 84-142 from an unidentified insertion sequence, and nt 143-447 from ret. The tyrosine kinase domain in the ret portion is said be constitutively active in the fusion product.

NCBI # NM\_005436 (SEQ ID NOs 162 and 163) relate to a human DNA segment, single copy, probe pH4 (transforming sequence, thyroid-1, (D10S170), mRNA. Nt 37-1794 are said to represent coding sequence, nt 202-996 said to encode a myosin tail, nt 610-999 an Ezrin/radixin/moesin family (ERM) region, with "a" and "c" allelic variation possible at nts 979, 1080, and 1445, and "a" and "g" possible at nt 1362, and "t" and "c" possible at nts 1996 and 2642.

NCBI # S77910 (SEQ ID NO 164) relates to H4= gene frequently rearranged with the ret proto-oncogene {promoter} [human, Genomic, 447 nt]. Nt 442-447 are said to correspond to the coding sequence, "MA".

NCBI # S72869 (SEQ ID NOs 165 and 166) relate to H4(D10S170)=putative cytoskeletal protein [human, thyroid, mRNA, 3011 nt]. Nt 37-1794 are said to correspond to coding sequence.

NCBI # X65617 (SEQ ID NO 167) relates to a human ret proto-oncogene DNA. Nt 1-54 are said to replace sequences from the H4 gene, nt 55-787 are said to correspond to an intron between the transmembrane and tyrosine kinase domain, and nt 788-808 said to correspond to an exon coding for a tyrosine kinase domain.

### **t(12;22)(q13;q12)**

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # NM\_005171 (SEQ ID NOs 168 and 169) relate to a human activating transcription factor 1 (ATF1), mRNA. Nt 157-252 are said to correspond to a pKID domain and nt 631-795 are said to correspond to a bZIP transcription factor region.

5 NCBI # AF047022 (SEQ ID NOs 170 and 171) relate to a human RNA binding protein-activating transcription factor-1 fusion protein (EWS-ATF1) mRNA, partial cds. Nt 1-65 are said to correspond to chromosome 22 and nt 66-353 to chromosome 12, with nt 66^67 said to represent the fusion junction between the EWS and ATF1 genes.

### **t(12; 16(q13; p11))**

10 This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # AJ301614 (SEQ ID NO 172) relates to a human t(12;16)(q13;p11) translocation breakpoint (CHOP/FUS chimaeric genomic DNA). Nt 1-225 are said to correspond to the CHOP gene (chromosome 12) and nt 226-500 to the FUS gene (chromosome 16).

15 NCBI # AJ301613 (SEQ ID NO 173) relates to a human t(12;16)(q13;p11) translocation breakpoint (FUS/CHOP chimaeric genomic DNA). Nt 1-317 are said to correspond to the FUS gene (chromosome 16) and nt 318-521 to the CHOP gene (chromosome 12).

20 NCBI # AJ301612 (SEQ ID NOs 174 and 175) relate human partial mRNA for FUS/CHOP chimaeric fusion protein (type 9 transcript variant). Nt 1-118 are said to originate from chromosome 16 and nt 119-225 are said to originate from chromosome 12.

NCBI # AJ301611 (SEQ ID NOs 176 and 177) relate to a human partial mRNA for FUS/CHOP chimaeric fusion protein (type 8 transcript variant). Nt 1-128 are said to originate from chromosome 16 and nt 129-235 are said to originate from chromosome 12.

25 NCBI # NM\_004960 (SEQ ID NOs 178 and 179) relate to a human fusion protein derived from t(12;16) malignant liposarcoma (FUS), mRNA. Nt 79-1659 are said to denote the coding sequence. Allelic variation is stated to be possible at nts 225 (a/c), 369 (c/t), and 1586 (a/g). Nt 937-1173 are said to denote an RNA recognition motif

(RRM), and nt 1354-1425 are said to denote a zinc finger domain in a Ran binding proteins (zf-Ranbp).

NCBI # S75762 (SEQ ID NOs 180 and 181) relate to a FUS...CHOP [human, myxoid liposarcoma specimens, mRNA Partial Mutant, 3 genes, 652 nt]. Nucleotides 1-272 are said to derive from FUS.

NCBI #X71427 (SEQ ID NOs 182 and 183) relate to a human mRNA for FUS-CHOP protein fusion. Nucleotides 70-1458 are said to denote the fusion coding sequence.

NCBI # X71428 (SEQ ID NOs 184 and 185) relate to a human mRNA for FUS glycine rich protein. Nucleotides 73-1650 are said to denote the coding sequence.

NCBI # Y10004 (SEQ ID NO 186) relates to a human DNA fragment containing fusion point of FUS gene and CHOP gene, translocation t(12;16)(q13;p11). The sequence is said to contain 5'-FUS intron 7 sequence and intron 1 3' sequence from CHOP.

NCBI # Y10003 (SEQ ID NO 187) relates to a human DNA fragment containing fusion point of FUS gene and CHOP gene, translocation t(12;16)(q13;p11). The sequence is said to contain 5'-FUS intron 7 sequence and intron 1 3' sequence from CHOP.

NCBI # Y10002 (SEQ ID NO 188) relates to a human DNA fragment containing fusion point of FUS gene and CHOP gene, translocation t(12;16)(q13;p11). The sequence is said to contain 5'-FUS intron 7 sequence and intron 1 3' sequence from CHOP.

NCBI # S75763 (SEQ ID NOs 189 and 190) relate to a FUS...CHOP [human, myxoid liposarcoma specimens, mRNA Partial Mutant, 3 genes, 377 nt]. Nt 1-272 are said to derive from FUS and nt 273-377 from CHOP.

### **t(2; 13)(q35;q14)**

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # U02308 (SEQ ID NOs 191 and 192) relate a human PAX-3-FKHR gene fusion mRNA, partial cds. Nt 1-2070 are said to be coding sequence.

**t(x; 18)(p11.2; q11.2)**

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # S79894 (SEQ ID NOs 193 and 194) relate to a SYT...SSX {translocation  
 5 breakpoint} [human, synovial sarcoma patient, tumor, mRNA Mutant, 3 genes, 165 nt].  
 Nt 1-18 are said to derive from SYT and nt 22-165 from SSX.

NCBI # X86175 (SEQ ID NOs 195 and 196) relate to a human mRNA for SSX2  
 protein. Nt 92-658 are said to be coding sequence.

10 The following chromosomal aberrations are not discussed in Figure 1 and will now  
 be discussed in more detail:

**t(12:21)(p13;q32)**

The TEL (ETV6)-AML1 (CBFA2) gene fusion is the most common reciprocal  
 chromosomal rearrangement in childhood cancer, occurring in approximately 25% of the  
 most predominant subtype of leukemia- common acute lymphoblastic leukemia. Ford et  
 15 al., Proc. Natl. Acad. Sci. U.S.A. 95 (8), 4584-4588 (1998), reported characterization of  
 the translocation event responsible for one TEL-AML1 genomic sequence in a pair of  
 monozygotic twins diagnosed at ages 3 years, 6 months and 4 years, 10 months with  
 common acute lymphoblastic leukemia. The twins shared an identical rearranged IgH  
 allele. These data have implications for the etiology and natural history of childhood  
 20 leukemia.

Other articles of interest on this subject include: Wiemels et al., *Protracted and  
 variable latency of acute lymphoblastic leukemia after TEL-AML1 gene fusion in utero*,  
 Blood. 1999 Aug 1;94(3):1057-62; Rubnitz et al., *The role of TEL fusion genes in  
 pediatric leukemias*, Leukemia, 1999 Jan;13(1):6-13. Review; Romana et al., *The t(12;21)  
 25 of acute lymphoblastic leukemia results in a tel-AML1 gene fusion*, Blood. 1995 Jun  
 15;85(12):3662-70; Seeger et al., *TEL-AML1 fusion in relapsed childhood acute  
 lymphoblastic leukemia*, Blood. 1999 94(1):374-6; Bayar et al., *Monozygotic twins with  
 congenital acute lymphoblastic leukemia (ALL) and t(4;11)(q21;q23)*, Cancer Genet  
 Cytogenet. 1996 Jul 15;89(2):177-80; Kobayashi et al., *Detection of the Der (21)t(12;21)*



chromosome forming the *TEL-AML1* fusion gene in childhood acute lymphoblastic leukemia, *Leuk Lymphoma*. 1997 Dec;28(1-2):43-50; and Shurtleff et al., *TEL/AML1 fusion resulting from a cryptic t(12;21) is the most common genetic lesion in pediatric ALL and defines a subgroup of patients with an excellent prognosis*, *Leukemia*, 1995 (12):1985-9.

NCBI# AF044317 (SEQ ID NO 197) relates to a human TEL/AML1 fusion gene, partial sequence. This was derived from an ALL infant. Nts 1-407 are said to derive from TEL and nts 408-548 from AML-1.

NCBI # AF231770 (SEQ ID NO 198) relates to a human ETV6/AML1 translocation breakpoint region.

#### **t(9;12)(q34; p13)**

In human leukemia, activation of the ABL proto-oncogene locus on chromosome 9 most commonly occurs as a result of its fusion to the BCR locus on chromosome. Papadopoulos et al., *Cancer Res.* 55 (1), 34-38 (1995), reported a t(9;12) event—a chimeric ABL protein displaying an elevated tyrosine kinase activity fused to a TEL protein from chromosome 12. Like BCR, TEL is fused in-frame with ABL and produces a fusion protein with an elevated tyrosine kinase activity when assayed in an immune complex. The amino-terminal sequences of TEL encodes a helix-loop-helix motif which may mediate dimerization. 43: *See also* Okuda et al., *Oncogene*. 1996 Sep 19;13(6):1147-52.

NCBI # Z36279 (SEQ ID NO 199) relates to a human (9TX) breakpoint position DNA for the tel-abl fusion identified by Papadopoulos et al. The translocation breakpoint is said to reside between nt 567 and 568.

#### **del(12p)**

Revy et al., *Cell* 102:565-575 (2000), reported hyper IgM immunodeficiencies associated with deletions of 19 and 9 bases at cDNA positions 21 and 175 respectively of the activation-induced cytidine deaminase (AID) gene. The former results in a 6 amino acid deletions and a phe15 to ter premature nonsense codon. The latter results in a 3-amino acid deletion and leu59-to -phe substitution.

NCBI # AB040430 (SEQ ID NOs 200 and 201) relate to a human AID gene for activation-induced cytidine deaminase, complete cds.

NCBI # AB040431 (SEQ ID NO 202 and 203) relate to a human AID mRNA for activation-induced cytidine deaminase, complete cds. Nt 77-673 is said to be coding  
5 sequence.

NCBI # NM\_020661 (SEQ ID NOs 204 and 205) relate to a human activation-induced cytidine deaminase (AICDA), mRNA. Nt 77-673 is said to be coding sequence. Allelic variation (a/g) is said to occur at nt 541.

**t(15;17)(q22;q12)**

10 de The et al., Cell 1991 Aug 23;66(4):675-84, reported a PML-RAR alpha fusion mRNA generated by a t(15;17) translocation associated with acute promyelocytic leukemia (APL). The gene product contained a novel zinc finger motif common to several DNA-binding proteins and the mRNA encoded a predicted 106 kd chimeric protein containing most of the PML sequences fused to a large part of RAR alpha, including its  
15 DNA- and hormone-binding domains. In transient expression assays, the hybrid protein exhibited altered transactivating properties if compared with the wild-type RAR alpha progenitor. Identical PML-RAR alpha fusion points were found in several patients, suggesting that in APL the t(15;17) translocation generates an RAR mutant that could contribute to leukemogenesis through interference with promyelocytic differentiation.

20 NCBI # S50916 (SEQ ID NOs 206 and 207) relate to a PML-RAR fusion gene {fusion transcript} [human, mRNA Partial, 1284 nt]. Nt 1-1251 is said to be coding sequence.

NCBI # M73779 (SEQ ID NOs 208 and 209) relate to a human PML-RAR protein (PML-RAR) mRNA, complete cds. Nt 67-2460 is said to be coding sequence.

25 NCBI # AJ417079 (SEQ ID NOs 210 and 211) relate to a human partial mRNA for PML/RARA fusion protein (PML/RARA gene). Nt 1-109 are said to derive from exon 6 of PML and nts 110-172 and 173-296 are said to derive from intron 2 and exon 3 of RARA.

**t(11;17)(q23;q12)**

Chen et al., EMBO J., 12 (3), 1161-1167 (1993), reported a fusion between a novel Kruppel-like zinc finger gene and the retinoic acid receptor-alpha locus due to a variant t(11;17) translocation associated with acute promyelocytic leukaemia (APL). Chen et al identified mRNAs containing the coding sequences of the new gene, fused in-frame either upstream of the RAR alpha B region or downstream from the unique A1 and A2 regions of the two major RAR alpha isoforms. The new gene, which Chen et al. termed PLZF (for promyelocytic leukaemia zinc finger), encodes a potential transcription factor containing nine zinc finger motifs related to the Drosophila gap gene Kruppel and is expressed as at least two isoforms which differ in the sequences encoding the N-terminal region of the protein. Within the haematopoietic system the PLZF mRNAs are detected in the bone marrow, early myeloid cell lines and peripheral blood mononuclear cells, but not in lymphoid cell lines or tissues. In addition, the PLZF mRNA levels were down-regulated in NB-4 and HL-60 promyelocytic cell lines in response to retinoic acid-induced granulocytic differentiation and were very low in mature granulocytes, suggesting an important role for PLZF as well as retinoic acid and its receptors in myeloid maturation.

NCBI # NM\_006006 (SEQ ID NOs 212 and 213) relate to a human zinc finger protein 145 (Kruppel-like, expressed in promyelocytic leukemia) (ZNF145), mRNA. Nt 76-2097 are said to be coding sequence.

NCBI # Z19002 (SEQ ID NOs 214 and 215) relate to a human PLZF gene encoding kruppel-like zinc finger protein. Nt 76-2097 are said to be coding sequence.

**t(16;16)(p13;q22) and inv(16)**

Springall et al., Leukemia 12 (12), 2034-2035 (1998), identified a novel CBFβ-MYH11 fusion transcript in a patient with AML and attributed it to an inversion/translocation of chromosome 16. *See also*, Krauter et al., Genes Chromosomes Cancer. 2001 Apr;30(4):342-8, *Detection and quantification of CBFβ/MYH11 fusion transcripts in patients with inv(16)-positive acute myeloblastic leukemia by real-time RT-PCR*; Martinelli et al., Haematologica. 2000 May;85(5):552-5, *Long-term disease-free acute myeloblastic leukemia with inv(16) is associated with PCR undetectable CBFβ/MYH11 transcript*; and Dierlamm et al., Genes Chromosomes Cancer. 1998

Jun;22(2):87-94. Review, *FISH identifies inv(16)(p13q22) masked by translocations in three cases of acute myeloid leukemia.*

NCBI # AF202996 (SEQ ID NOs 216 and 217) relate to a human core binding factor beta-smooth muscle myosin heavy chain fusion protein (CBFB-MYH11) mRNA, partial cds. Nt 1-46 are said to originate from 16q22 and nt 47-89 are said to originate from 16p13. Nt 50 is said to be a "t" in some reports.

NCBI # AF251768 (SEQ ID NOs 218 and 219) relate to human PCFBF/MYH11E chimeric fusion protein (CBFB/MYH11) mRNA, partial cds. Nt 1-42 are said to derive from exon 5 of CBFB and nts 42-78 from exon 7 of MYH11.

NCBI # AF249898 (SEQ ID NOs 220 and 221) relate to a human PCBFbeta/MYH11A chimeric fusion protein (CBFbeta/MYH11A) mRNA, partial cds. Nt 1-42 are said to derive from exon 5 of CBFB and nts 42-78 from exon 12 of MYH11.

NCBI # AF249897 (SEQ ID NOs 222 and 223) relate to a human s PCBFb-MYH11d chimeric fusion protein (CBFB/MYH11D) mRNA, partial cds.

NCBI # AF390860 (SEQ ID NO 224) relates to a human UPN2 CBFB/MYH11 translocation breakpoint region sequence.

NCBI # AF390859 (SEQ ID NO 225) relates to a human isolate UPN1 CBFB/MYH11 translocation breakpoint region sequence.

### **t(9;11)(p22;q23)**

Tkachuk et al., Cell 71: 691-700, (1992), showed that the gene involved in recurring 11q23 leukemogenic translocations codes for an unusually large protein that is a homolog of Drosophila 'trithorax' and is involved in homeotic gene regulation (MLL; aka ALL1). In studies of a t(11;19) translocation, they identified a chimeric protein containing the amino-terminal 'AT-hook' motifs of the MLL gene on chromosome 11 fused to a previously undescribed protein from chromosome 19. The nucleotide sequence determinations demonstrated an open reading frame that coded for a predicted 62-kD protein, which Tkachuk et al. named ENL.

Nakamura et al., Proc. Nat. Acad. Sci. 90: 4631-4635, (1993), showed that the gene on chromosome 19 that is fused to the MLL gene in patients with leukemia and translocation t(11;19)(q23;p13) shows high sequence homology to the genes on chromosome 4 and chromosome 9 that are fused with the ALL1 gene in patients with translocation t(4;11)(q21;q23) and t(9;11)(p22;q23), respectively. The 3 protein gene products contained nuclear targeting sequences as well as serine-rich and proline-rich regions. The results suggested that the different proteins fused to ALL1 polypeptides. These leukemias provide similar functional domains.

Negrini et al., Cancer Res 1993 Oct 1;53(19):4489-92, reported potential topoisomerase II DNA-binding sites at the breakpoints of a t(9;11) chromosome translocation in acute myeloid leukemia. The event examined was a t(9;11)(p22;q23) chromosome translocation and the breakpoints on the two chromosomes occurred within introns of the involved genes: AF-9 on chromosome 9, and ALL-1 on chromosome 11. Sequence analysis identified heptamers flanking the breakpoints on both chromosomes 9 and 11, suggesting that the V-D-J recombinase was involved in the translocation. See also Cimino et al., Cancer Res. 1991 Dec 15;51(24):6712-4, *Cloning of ALL-1, the locus involved in leukemias with the t(4;11)(q21;q23), t(9;11)(p22;q23), and t(11;19)(q23;p13) chromosome translocations.*

Poirel et al., Blood 87 (6), 2496-2505 (1996), reported an MLL-AF9=fusion gene {fusion site} [human, peripheral blood, acute myeloid leukemia FAB type M1 patient UPN 427, mRNA Partial, 60 nt]; NCBI # S82034 (SEQ ID NO 226), and indicated the breakpoint to be at nucleotide 29.

#### **t(1;22)(p13;q13)**

Nakamura et al., Proc Natl Acad Sci U S A 1993 May 15;90(10):4631-5, correlated aberrations on chromosomes 4, 9, and 19 involved in 11q23 abnormalities in acute leukemia with shared sequence homology and/or common motifs, including fusions of the ENL gene with ALL-1 in (11;19) translocations. ENL proteins contain nuclear targeting sequences as well as serine-rich and proline-rich regions. Stretches abundant in basic amino acids are also present.

NCBI # AF364037 (SEQ ID NOs 227 and 228) relate to a human megakaryoblastic leukemia-1 protein/RNA-binding motif protein 15s + ae fusion protein (MKL1/RBM15 fusion) mRNA, complete cds. Ma et al., Nat. Genet. 28 (3), 220-221 (2001) identified this with an acute megakaryoblastic leukemia patient. Nt 144-221 are said to be coding sequence, with nts 1-150 deriving from chromosome 22 and nts 151-300 deriving from chromosome 1.

### **t(3;3)(q21;q26) or inv(3)(q21q26)**

Ogawa et al., Oncogene 1996 Jul 4;13(1):183-91 showed that overexpression of the Evi-1 gene appears to be a consistent feature of the 3q21q26 syndrome, an association of myeloid leukemias/myelodysplastic syndrome with a specific chromosomal aberration involving both 3q21 and 3q26, such as t(3;3)(q21;q26) or inv(3)(q21q26). The rearrangement in 3q26 has been reported to occur near the Evi-1 locus, implicating that it is the critical gene deregulated in the 3q21q26 syndrome. Ogawa identified a structural abnormality of Evi-1 protein in a case with the 3q21q26 syndrome. That case carried the typical inv(3)(q21q26), in which the 3q26 breakpoint is located within an intron of the Evi-1 gene, and resulted in overexpression of a normally unexpressed, aberrant form of Evi-1 protein, in which the C-terminal 44 amino acids of wild-type Evi-1 protein were truncated and replaced by five amino acids. The truncated Evi-1 protein was shown to increase AP1 activity when expressed in NIH3T3 cells as its wild-type counterpart. The origin of this peculiar type of rearrangement of the Evi-1 gene was shown not to be an artifact during establishment of the cell line, but rather an event that occurred in the primary leukemic cells, and consistent with 3q21q26 syndrome.

NCBI # S82592 (SEQ ID NOs 229 and 230) relate to an Evi-1=Evi-1 protein {3' region, deletion region} [human, megakaryoblastoid cell line MOLM-1, chronic myelocytic leukemia patient, mRNA Partial Mutant, 916 nt]. Nt 1-132 are said to represent a partial coding sequence.

### **t(3;5)(q25;q34)**

Yoneda-Kato et al., Oncogene 12: 265-275 (1996), showed that t(3;5)(q25.1;q34) of myelodysplastic syndrome and acute myeloid leukemia produces a novel fusion gene, NPM-MLF1, which results from an in-frame fusion between the 5-prime coding region of

the nucleophosmin gene on chromosome 5 and a gene on chromosome 3, designated MLF1 (myeloid leukemia factor-1). The translocation was identified in 3 t(3;5)-positive cases of AML. Expression of the mRNA was widespread but highest in testis, ovary, skeletal muscle, heart, kidney and colon. Antibodies to MLF1 detected a 31-kD protein in K562 and HEL erythroleukemia cell lines

NCBI # L49054 (SEQ ID NOs 231 and 232) relate to a t(3;5)(q25.1;p34) fusion gene NPM-MLF1 mRNA, complete cds. Nt 109-915 are said to be coding sequence.

NCBI # BC007045 (SEQ ID NOs 233 and 234) relate to a human myeloid leukemia factor 1, clone MGC:12449, mRNA, complete cds. Nt 107-913 are said to be coding sequence.

NCBI # L49054 (SEQ ID NOs 235 and 236) relate to a human t(3;5)(q25.1;p34) fusion gene NPM-MLF1 mRNA, complete cds. Nt 109-915 are said to be coding sequence.

#### **t(7;11)(p15;p15)**

Borrow et al., Nat. Genet. 1996 Feb;12(2):159-67, reported a t(7;11)(p15;p15) translocation in acute myeloid leukaemia that fused the genes for nucleoporin NUP98 and class I homeoprotein HOXA9.

NCBI # U41814 (SEQ ID NOs 237 and 238) relate to human NUP98-HOXA9 fusion protein mRNA, partial cds. Nt 46^47 are said to represent a NUP98-HOXA9 in-frame junction and nt 138^139 are said to be an alternative splice site within HOXA9

NCBI # NM\_002142 (SEQ ID NOs 239 and 240) relate to a human homeo box A9 (HOXA9), mRNA. Nts 67 and 213 are said to have allelic variation possible (c/g), and nt 397-567 and 397-576 are said to respectively represent a homeobox domain and a homeodomain (HOX region).

NCBI # U81511 (SEQ ID NOs 241, 242, and 243) relate to a human HOXA-9A and HOXA-9B (HOXA-9) gene, alternatively spliced, complete cds. Nts 145-502, 4327-4894, and 5893-6131 are said to be exon (coding) sequences, with introns present at 503-5892 and 4895-5892. Alternative splicing events are said to account for the overlap.

**t(8;16)(p11;p13)**

Panagopoulos et al., Genes Chromosomes Cancer. 2000 Aug;28(4):415-24, used RT-PCR analysis to identify MOZ-CBP and CBP-MOZ chimeric transcripts in acute myeloid leukemias with t(8;16)(p11;p13) translocations.

5 NCBI # AJ251844 (SEQ ID NOs 244 and 245) relate to human partial mRNA for MOZ/CBP chimeric transcript type II. Nt 1-188 are said to derive from chromosome 8 and nts 189-415 from chromosome 16.

NCBI # AJ251845 (SEQ ID NOs 246 and 247) relate to a human partial mRNA for CBP/MOZ chimeric transcript. Nt 1-110 are said to derive from chromosome 16 and nts  
10 111-229 from chromosome 8.

NCBI # AJ251843 (SEQ ID NOs 248 and 249) relate to human partial mRNA for MOZ/CBP chimeric transcript type I. Nt 1-188 are said to derive from chromosome 8 and nts 189-1128 from chromosome 16.

NCBI # U47742 (SEQ ID NOs 250 and 251) relate to human monocytic leukaemia  
15 zinc finger protein (MOZ) mRNA, complete cds.

NCBI # U85962 (SEQ ID NOs 252 and 253) relate to a human CREB-binding protein mRNA, complete cds. Nt 814-8147 are said to contain coding sequence and nts 819-1124 are said to encode a nuclear receptor binding domain.

**t(9;12)(q34;p13)**

20 Papadopoulos et al., Cancer Res. 1995 Jan 1;55(1):34-8, reported activation of ABL by fusion to an ets-related gene, TEL.

NCBI # Z35761 (SEQ ID NOs 254 and 255) relate to a human TEL/ABL fusion protien. Nt 1-463 are said to contain a partial TEL sequence and nt 464-549 are said to contain ABL sequence.

25 NCBI # Z36279 (SEQ ID NO 256) relates to human (9TX) breakpoint position DNA. The breakpoint position is said to reside at 567..568.



NCBI # Z36278 (SEQ ID NO 257) relates to human (boucher) breakpoint position DNA. The breakpoint position is said to reside at 567..568.

**t(12;22)(p13;q13)**

Buijs et al., *Oncogene*. 1995 Apr 20;10(8):1511-9, reported that a t(12;22) (p13;q11) event resulted in a myeloproliferative disorders characterized by the fusion of the ETS-like TEL gene on 12p13 to the MN1 gene on 22q11.

NCBI # X85024 (SEQ ID NOs 258 and 259) relate to a human mRNA for TEL-MN1 fusion gene (type II). Nt 22..23 is said to be the fusion site.

NCBI # X85026 (SEQ ID NOs 260 and 261) relate to a human mRNA for a TEL-MN1 fusion gene (type I). Nt 22..23 is said to be the fusion site.

NCBI # X85027 (SEQ ID NOs 262 and 263) relate to a human mRNA for a MN1-TEL fusion gene (type II). Nt 22..23 is said to be the fusion site.

NCBI # X85025 (SEQ ID NOs 264 and 265) relate to a human mRNA for a MN1-TEL fusion gene (type I). Nt 22..23 is said to be the fusion site.

**15 del(5q)**

Jaju et al., *Blood* 1999 Jul 15;94(2):773-80, reported a recurrent translocation, t(5;11)(q35;p15.5), associated with a del(5q) in childhood acute myeloid leukemia. Partial deletion of the long arm of chromosome 5, del(5q), is the cytogenetic hallmark of the 5q-syndrome, a distinct subtype of myelodysplastic syndrome-refractory anemia (MDS-RA). Deletions of 5q also occur in the full spectrum of other de novo and therapy-related MDS and acute myeloid leukemia (AML) types, most often in association with other chromosome abnormalities. However, the loss of genetic material from 5q is believed to be of primary importance in the pathogenesis of all del(5q) disorders.

Lindgren et al., *Am J Hum Genet* 1992 May;50(5):988-97, reported phenotypic, cytogenetic, and molecular studies of three patients with constitutional deletions of chromosome 5 in the region of the gene for familial adenomatous polyposis, APC, affiliated with colon cancer and polyps. High-resolution banding studies indicated that some deletions spans the region 5q21-q22..

Other potential deletion aberrations at the 5q locus include but are not limited to deletions at positions 5q13.3, corresponding to the RASA1 gene encoding the GAP RAS p21 protein activator 1 (GTPase activating protein), aberrancies of which are known to associate with basal cell carcinoma; 5q21, corresponding to the PST gene encoding PST1 Polysialyltransferase; 5q21-q22, corresponding to the APC gene, aberrancies of which correlate with colorectal cancer; 5q31, corresponding to the FACL6 gene encoding ACS2 Fatty-acid-Coenzyme A ligase, a long-chain 6 (long-chain acyl-CoA synthetase 2), aberrancies of which give rise to myelodysplastic syndrome and acute myelogenous leukemia; 5q31, encoding the GRAF GTPase regulator associated with the focal adhesion kinase, aberrancies of which give rise to juvenile myelomonocytic leukemia; 5q31.1, encoding IRF1, a MAR Interferon regulatory factor-1, aberrancies of which give rise to macrocytic anemiam myelodysplastic syndrome (preleukemic), acute myelogenous leukemia, gastric cancer, and nonsmall cell lung cancer; 5q33.2-q33.3, corresponding to CSF1R, FMS Colony-stimulating factor-1 receptor, aberranceis of which have been associated with oncogene FMS (McDonough feline sarcoma), and predisposition to myeloid malignancy; 5q35, encoding NPM1 Nucleophosmin 1 (nucleolar phosphoprotein B23, numatrin), aberrancies of which are known to associate with acute promyelocytic leukemia; 5q35.3, encoding gene FLT4, VEGFR3, encoding PCL fms-related tyrosine kinase-4 (vascular endothelial growth factor receptor, aberrancies of which contribute to hereditary lymphedema.

NCBI # NM\_002387 (SEQ ID NOs 266 and 267) relate to a human gene that is found mutated in colorectal cancers(MCC) mRNA. Nt 221-2710 are said to represent coding sequence. Allelic variation is said to exist at nt 2869 (c/t).

#### **del(7q)**

Schwartz et al., Cytogenet. Cell Genet. 51: 152-153 (1991) reported deletion mapping of plasminogen activator inhibitor, type I (PLANH1) and beta-glucuronidase (GUSB) in 7q21-q22. Wedemeyer et al., Genomics 46: 313-315 (1997) reported the proximity of the human HIP1 gene close to the elastin (ELN) locus on 7q11.23. Dridi et al., Am. J. Med. Genet. 87: 134-138 (1999), reported skin elastic fibers in Williams syndrome and Dutly et al., Am. J. Med. Genet. 87: 134-138 (1999), reported unequal interchromosomal rearrangements corresponding to deletions in these genes, and affiliated

with Williams-Beuren syndrome. Naritomi et al., Hum. Genet. 80: 201-202 (1988), reported a microdeletion of the proximal long arm of chromosome 7 affiliated with Zellweger syndrome. Horiike et al., Leukemia. (1999) Aug;13(8):1235-42, reported distinct genetic involvement of the TP53 gene in therapy-related leukemia and myelodysplasia, with chromosomal 7 losses and their possible relationship to replication error phenotype and the development of therapy-related AML/MDS. Wong et al., Cancer Genet Cytogenet. 1995 Jul 1;82(1):70-2, reported biclonal acute monoblastic leukemia associated with del(7q). Particular sites of interest include 7q11.23, encoding PTPN12, PTPG1 Protein tyrosine phosphatase, nonreceptor-type, known to associate with colon cancer; 7q21-q22, encoding PEX1, ZWS1 Peroxisome biogenesis factor-1, associate with Zellweger syndrome-1, neonatal adrenoleukodystrophy and infantile Refsum disease; 7q22-q31.1, encoding SLC26A3, DRA, CLD Solute carrier family 26 (sulfate transporter), member 3, associated with colon cancer; 7q31-q32 SMOH, SMO Smoothed, Drosophila, homolog of 601500, associated with sporadic basal cell carcinoma.

#### **del(20q)**

A deletion in the long arm of chromosome 20 is a recurring abnormality in malignant myeloid disorders. Its occurrence suggests that the loss of genetic material on 20q provides a proliferative advantage to myeloid cells, possibly through the loss of a tumor-suppressor gene. Roulston et al., Blood 82: 3424-3429 (1993), examined a series of patients with the del(20q) using fluorescence in situ hybridization with unique sequence probes that map along the length of 20q and delineated a segment that is deleted in 95% of all patients they examined (18 of 19). In addition, they showed that the deletions are interstitial rather than terminal. The region of deletion extended from 20q11.2 to 20q12 and was flanked by RPN2 (180490) proximally and D20S17 distally. The SRC (190090) and ADA (102700) genes were found to be located within the commonly deleted segment.

Stoffel et al. (1996) generated a YAC contig map of 20q11.2-q13.1 in a region spanning about 18 Mb and representing about 40% of the physical length of 20q. The map contains the chromosomal regions deleted in MODY1 (125850) and in myeloid leukemia. Using this physical map, they refined the location of a myeloid tumor suppressor-related gene to an 18-cM interval (approximately 13 Mb) between RPN2 and D20S17.

Stoffel et al., Proc. Nat. Acad. Sci. 93: 3937-3941 (1996), correlated the occurrence of del(20q) in a broad spectrum of myeloid disorders, suggesting that the loss of genetic material on 20q could provide a proliferative advantage to myeloid cells, possibly through the loss of a tumor-suppressor gene. Stoffel et al. examined a series of patients with the del(20q) using fluorescence in situ hybridization (FISH) with unique sequence probes that map along the length of 20q, delineated a segment that is deleted in 95% of all patients examined (18 of 19), and showed that the deletions are interstitial rather than terminal. This region of deletion extends from 20q11.2 to q12, and is flanked by the RPN2 (proximal) and D20S17 loci (distal). The SRC and ADA genes are located within the commonly deleted segment.

#### **t(11q23)**

Shiah et al., Leukemia, (2002) 16(2):196-202, reported clinical and biological implications of partial tandem duplication of the MLL gene in acute myeloid leukemia without chromosomal abnormalities at 11q23. The clinical and biological features of acute myeloid leukemia (AML) with 11q23/MLL translocations are well known, but the characteristics of AML with partial tandem duplication of the MLL gene have not been explored comprehensively. Sheah et al analyzed MLL duplication in 81 AML patients without chromosomal abnormalities at 11q23, using Southern blotting, genomic DNA polymerase chain reaction (PCR), reverse-transcription PCR and complementary DNA sequencing. Nine patients showed partial tandem duplication of the MLL gene, including eight (12%) of the 68 with normal karyotype. Seven patients showed fusion of exon 6/exon 2 (e6/e2), one, combination of differentially spliced transcripts e7/e2 and e6/e2, and the remaining one, combination of e8/e2 and e7/e2. Among the patients with normal karyotype, children aged 1 to 15 showed a trend to higher frequency of MLL duplication than other patients (2/5 or 40% vs 6/62 or 10%,  $P = 0.102$ ). The patients with tandem duplication of the MLL gene had a significantly higher incidence of CD11b expression on leukemic cells than did those without in the subgroup of patients with normal karyotype (75% vs 28%,  $P = 0.017$ ). There were no significant differences in the expression of lymphoid antigens or other myeloid antigens between the two groups of patients. In adults, the patients with MLL duplication had a shorter median survival time than those without (4.5 months vs 12 months,  $P = 0.036$ ). In conclusion, partial tandem duplication of the MLL gene is associated with increased expression of CD11b on leukemic blasts and

implicates poor prognosis in adult AML patients. The higher frequency of MLL duplication in children older than 1 year, than in other age groups, needs to be confirmed by further studies.

Ono et al., Cancer Res. 2002 Jan 15;62(2):333-7, reported that SEPTIN6, a human  
5 homologue to mouse Septin6, is fused to MLL in infant acute myeloid leukemia with complex chromosomal abnormalities involving 11q23 and Xq24.

Borkhardt et al., Genes Chromosomes Cancer. 2001 Sep;32(1):82-8, reported an ins(X;11)(q24;q23) that fuses the MLL and the Septin 6/KIAA0128 gene in an infant with AML-M2.

10 Luo et al., Mol Cell Biol. 2001 Aug;21(16):5678-87, reported that ELL-associated factor 1 interaction domain is essential for MLL-ELL-induced leukemogenesis.

Kuwada et al., Cancer Res. 2001 Mar 15;61(6):2665-9, reported a t(11;14)(q23;q24) that generates an MLL-human gephyrin fusion gene along with a de facto truncated MLL in acute monoblastic leukemia.

15 Garcia-Cuellar et al., Oncogene. 2000 Mar 30;19(14):1744-51, reported that ENL, the MLL fusion partner in t(11;19), binds to the c-Abl interactor protein 1 (ABI1) that is fused to MLL in t(10;11)+.

Akao et al., Genes Chromosomes Cancer. 2000 Apr;27(4):412-7, reported an analysis of the rearranged genome and chimeric mRNAs caused by a t(6;11)(q27;q23)  
20 chromosome translocation involving MLL in an infant acute monocytic leukemia.

Hayashi et al., Cancer Res. 2000 Feb 15;60(4):1139-45, reported a leukemic cell line, SN-1, associated with a t(11;16)(q23;p13).

So et al., Cancer Genet Cytogenet. 2000 Feb;117(1):24-7, analysed MLL-derived transcripts in an infant acute monocytic leukemia having a complex translocation  
25 (1;11;4)(q21;q23;p16).

Kourlas et al., Proc Natl Acad Sci U S A. 2000 Feb 29;97(5):2145-50, identified a gene at 11q23 encoding a guanine nucleotide exchange factor that fuses with MLL in acute myeloid leukemia.

Taki et al., Proc Natl Acad Sci U S A. 1999 Dec 7;96(25):14535-40, reported that AF5q31, an AF4-related gene, is fused to MLL in infant acute lymphoblastic leukemia with an ins(5;11)(q31;q13q23).

Taki et al., Cancer Res. 1999 Sep 1;59(17):4261-5, reported that AF17q25, a putative septin family gene, fuses with the MLL gene in acute myeloid leukemia associated with a t(11;17)(q23;q25).

Busson-Le Coniat et al., Leukemia. 1999 Feb;13(2):302-6, reported MLL-AF1q fusion resulting from t(1;11) in an acute leukemia.

Slany et al., Mol Cell Biol. 1998 Jan;18(1):122-9, reported on the oncogenic capacity of HRX-ENL that requires the transcriptional transactivation activity of ENL and the DNA binding motifs of HRX.

Other articles of interest include, Super et al., Genes Chromosomes Cancer. 1997 Oct;20(2):185-95, *Identification of complex genomic breakpoint junctions in the t(9;11) MLL-AF9 fusion gene in acute leukemia*; Taki et al., Blood. 1997 Jun 1;89(11):3945-50, *The t(11;16)(q23;p13) translocation in myelodysplastic syndrome fuses the MLL gene to the CBP gene*; Taki Tet al., *Fusion of the MLL gene with two different genes, AF-6 and AF-5alpha, by a complex translocation involving chromosomes 5, 6, 8 and 11 in infant leukemia*, Oncogene. 1996 Nov 21;13(10):2121-30. Tanabe et al., *AF10 is split by MLL and HEAB, a human homolog to a putative Caenorhabditis elegans ATP/GTP-binding protein in an inv(10;11)(p12;q23q12)*, Blood. 1996 Nov 1;88(9):3535-45; Ma et al., *LAF-4 encodes a lymphoid nuclear protein with transactivation potential that is homologous to AF-4, the gene fused to MLL in t(4;11) leukemias*, Blood. 1996 Jan 15;87(2):734-45; Prasad et al., *Domains with transcriptional regulatory activity within the ALL1 and AF4 proteins involved in acute leukemia*, Proc Natl Acad Sci U S A. 1995 Dec 19;92(26):12160-4. Baffa et al., *Involvement of the ALL-1 gene in a solid tumor*, Proc Natl Acad Sci U S A. 1995 May 23;92(11):4922; Mitani, *Cloning of several species of MLL/MEN chimeric cDNAs in myeloid leukemia with t(11;19)(q23;p13.1) translocation*, Blood. 1995 Apr 15;85(8):2017-24; Tse et al., *A novel gene, AF1q, fused to MLL in t(1;11) (q21;q23), is specifically expressed in leukemic and immature hematopoietic cells*, Blood. 1995 Feb 1;85(3):650-6; Chen et al., *Acute promyelocytic leukemia: from clinic to molecular biology*, Stem Cells. 1995 Jan;13(1):22-31. Review; Rubnitz et al., *ENL, the*

- gene fused with HRX in t(11;19) leukemias, encodes a nuclear protein with transcriptional activation potential in lymphoid and myeloid cells, *Blood*. 1994 Sep 15;84(6):1747-52; Prasad et al., *Leucine-zipper dimerization motif encoded by the AF17 gene fused to ALL-1 (MLL) in acute leukemia*, *Proc Natl Acad Sci U S A*. 1994 Aug 16;91(17):8107-11;
- 5 Meerabux et al., *Molecular cloning of a novel 11q23 breakpoint associated with non-Hodgkin's lymphoma*, *Oncogene*. 1994 Mar;9(3):893-8; Gauwerky et al., *Chromosomal translocations in leukaemia*, *Semin Cancer Biol*. 1993 Dec;4(6):333-40. Review; Hunger et al., *HRX involvement in de novo and secondary leukemias with diverse chromosome 11q23 abnormalities*, *Blood*. 1993 Jun 15;81(12):3197-203; Morrissey et al., *A*
- 10 *serine/proline-rich protein is fused to HRX in t(4;11) acute leukemias*, *Blood*. 1993 Mar 1;81(5):1124-31; Tkachuk et al., *Involvement of a homolog of Drosophila trithorax by 11q23 chromosomal translocations in acute leukemias*, *Cell*. 1992 Nov 13;71(4):691-700.

#### **t(5;12)(q31;p13)**

- Yagasaki et al. described a fusion of LACS to a TEL/ETV6 gene in an acute
- 15 myeloblastic leukemia case having a t(5;12) chromosomal translocation. The human mRNA fusion sequence may be found in NCBI # AF102845 (SEQ ID NO 268). Nt 1-40 are said to derive from the TEL gene on chromosome 12 and nt 41-1172 are said to derive from the LACS gene on chromosome 5.

#### **t(1;12)(q25;p13)**

- Cazzaniga et al., *Blood* 94: 4370-4373 (1999), reported an instance of the tyrosine kinase Abl-related gene ARG fused to ETV6 in an AML-M4Eo patient having a
- t(1;12)(q25;p13) translocation, and cloned reciprocal chimeric transcripts associated with the event. The ETV6/TEL gene is rearranged in most patients with 12p13 translocations fused to a number of different partners. One of the chimeric proteins consisted of the
- 25 helix-loop-helix oligomerization domain of ETV6 and the SH2, SH3, and protein tyrosine kinase domains of ABL2. The reciprocal transcript ABL2-ETV6 was also detected in the patient's RNA by RT-PCR, although at a lower expression level.

**t(12;15)(p13;q25)**

Wai et al., *Oncogene*. 2000 Feb 17;19(7):906-15, reported an ETV6-NTRK3 gene fusion associated with such translocation.

Eguchi et al., *Blood*. 1999 Feb 15;93(4):1355-63, reported a similar fusion of ETV6 to neurotrophin-3 receptor TRKC in acute myeloid leukemia with t(12;15)(p13;q25).

Knezevich et al., *Nat Genet*. 1998 Feb;18(2):184-7; reported an ETV6-NTRK3 gene fusion in congenital fibrosarcoma.

NCBI # AF125808 (SEQ ID NOs 269 and 270) relate to a human ETS related protein-neurotrophic receptor tyrosine kinase fusion protein (ETV6-NTRK3 fusion) mRNA, partial cds. Nt 12-64 are said to derive from chromosome 12 and nt 65-980 from chromosome 15.

NCBI # AF041811 (SEQ ID NOs 271 and 272) relate to a human ETS related protein-growth factor receptor tyrosine kinase fusion proteins (ETV6-NTRK3 fusion) mRNA, partial cds. . Nt 1-336 are said to derive from chromosome 12 and nt 337-1403 from chromosome 15.

**t(1;12)(q21;p13)**

Salomon-Nguyen et al., *Proc Natl Acad Sci U S A*. (2000) 97(12):6757-62, reported a t(1;12)(q21;p13) translocation observed in a case of acute myeloblastic leukemia (AML-M2). At the protein level, the untranslocated TEL copy and, as a result of the t(1;12) translocation, a fusion protein containing the amino-terminal part of TEL and essentially all of the ARNT gene (126110), were expressed. The TEL/ETV6 gene is located at 12p13 and encodes a member of the ETS family of transcription factors. Translocated ETS leukemia (TEL) is frequently involved in chromosomal translocations in human malignancies, usually resulting in the expression of fusion proteins between the amino-terminal part of TEL and either unrelated transcription factors or protein tyrosine kinases. ARNT (aryl hydrocarbon receptor nuclear translocator) belongs to a subfamily of the "basic region helix-loop-helix" (bHLH) protein that shares an additional region of similarity called the PAS (Per, ARNT, SIM) domain. ARNT is the central partner of



several heterodimeric transcription factors, including those containing the aryl hydrocarbon (dioxin) receptor (AhR) and the hypoxia-inducible factor 1 alpha (HIF1alpha). Interference with the activity of AhR or HIF1alpha may contribute to leukemogenesis.

## 2. Mutant Protein or Cellular Protein Isoforms

The second group of target proteins are mutants or isoforms (*e.g.* splice variants) of normal cellular proteins (usually the products of tumor suppressor genes) that, due to their mutant nature, exhibit a heightened dependence on HSP90 chaperone functions or else increased sensitivity, *i.e.*, instability, due to HSP90 inhibitors. The mutant or isoform proteins either (a) have become overtly oncogenic (a “dominant-positive” (DP) effect), or (b) exert a “dominant-negative” (DN) effect on their normal counterpart, thus preventing the normal protein’s tumor suppressor activity, and resulting in a net oncogenic effect. The examples are largely illustrated with respect to human sequences, although the person of ordinary skill will appreciate that homologs in other organisms are likewise included within the purview of the invention.

### a. v-src

One such example of a mutant or isoform protein is human v-src (NCBI #s NM\_005417; SEQ ID NOs 273 and 274 ), which counterpart, c-src (NCBI # XM\_044659 (SEQ ID NOs 275 and 276), corresponds to the normal cellular gene product. As described above, proteins with a heightened dependence on HSP90 can be identified by their enhanced sensitivity to degradation induced by HSP90 inhibitors, such as the ansamycin antibiotic geldanamycin. Ansamycins and other HSP90 inhibitors were originally isolated on the basis of their ability to revert v-src transformed fibroblasts (Uehara, Y. *et al.*, 1985, *Supra*, 76: 672-675) and this reversal was correlated with the functional inactivation of the v-src protein (Uehara, Y. *et al.*, 1986, *Mol. Cell. Biol.*, 6: 2198-2206). This effect was subsequently reported to be caused by the ubiquitin/proteasome-dependent degradation of the transforming v-src protein as a result of inhibition of HSP90 function by geldanamycin (Whitesell, L., *et al.*, 1994, *supra*). Finally, a recent study compared the rate and potency of degradation of v-src and c-src proteins after treatment of Rous sarcoma virus-transformed 3T3 fibroblasts with the ansamycin geldanamycin. In this study, the oncogenic mutant v-src protein was almost 100% degraded within 6 hours (An, W *et al.*, 2000, *supra*, see Figure 2), whereas the normal cellular counterpart, c-src, was largely unaffected even after 20 hours of the same treatment (An, W *et al.*, 2000, *supra*, see Figure 4).

HSP90 inhibitors can selectively induce degradation of a wide range of mutated or otherwise aberrant proteins that cause or exacerbate a disease, and that have an apparent heightened dependence on HSP90.

**b. RET**

5 An example of a dominant proto-oncogene encoding a signaling protein that is mutated in certain human cancers giving rise to constitutively active structurally abnormal cellular proteins is the *RET* proto-oncogene (NCBI # P07949; SEQ ID NO 277) in multiple endocrine neoplasia Type 2 (MEN-2). *RET* encodes a receptor tyrosine kinase whose ligand is presently unidentified (Kolibaba, K, *et al*, 1997, *Supra*). The germline mutations found in MEN-2A patients (Cys634→  
10 Arg/Tyr, similar mutations at Cys609, 611, 618 and 620) alter the tertiary structure of the protein resulting in homodimerization and activation of the kinase domain. The commonly observed mutation in MEN-2B, Met918→Thr, alters the kinase domain structure, causing activation directly. Both of these pathways involve alterations in protein conformation, which again implicates HSP90 and underscores the broad utility of the invention.

**c. p53**

15 Another example of a mutant, oncogenic variant group of a normal cellular protein is tumor suppressor antigen p53. The wild-type protein and mRNA sequences for p53 are found in NCBI accession # M14695 (SEQ ID NOs 278 and 279). However, numerous mutations in p53 are known to occur and represent the most common molecular genetic defects found in human  
20 cancers (Harris, C *et al*, 1993, *N. Engl. J. Med.* 329:1318-1327). A mutant p53 protein was reportedly degraded in cells following treatment with geldanamycin, but wild type p53 exhibited no such, or only minimal, degradation (Blagosklonny, M *et al*, 1995, *Oncogene*, 11:933-939). Unlike the situation described above for v-src, most p53 mutations are “loss of function” effects , *i.e.*, the mutation results in the inability of the protein to perform one or more of its normal  
25 functions. Thus, in a tumor cell that has an intact p53 allele and a loss of function mutant allele, simply causing the mutant form to be degraded will not change cellular behavior. However, if the mutant protein by some mechanism inhibits the action of its coexpressed normal counterpart inside tumor cells, then degrading it will affect cellular behaviour.

This “dominant-negative” (DN) effect has been shown to occur in cells harboring certain  
30 p53 mutants, and by several different mechanisms. For example, a mutant may afford tighter

DNA binding without transactivation (Chene, P, *et al*, 1999, *Int. J. Cancer*. 82:17-22). This type of p53 mutant does not exhibit “classical” DN activity unless the mutation confers an increased affinity for DNA, because the mutant stoichiometrically competes with the wild type (WT) protein for binding to DNA. Another example is inhibition of tetramerization by incorporation of one or more mutant p53s into a complex with WT proteins (Deb, D *et al*, 1999, *Int. J. Oncol.* 15:413-422, Rollenhagen, C *et al*, 1998, *Int. J. Cancer* 78:372-376). Yet a third example concerns “prion-like” activity, in which a mutant protein forces a WT protein into a mutant conformation that then impairs its ability to bind to DNA and/or transactivate p53 target genes (Chene, P, 1998, *J. Mol. Biol.* 281:205-209)

Increased stability of mutants relative to WT proteins causes them to accumulate and override normal p53 biology. This is counterintuitive given the fact that p53 has a built-in negative feedback loop on its own transcription (via induction of the mdm-2 protein, which subsequently targets p53 for degradation). If the increased stability of a given mutant were due solely to failure to transactivate mdm-2, then accumulation of the mutant would not occur in the presence of a WT allele (Blagosklonny, M, 2000, *FASEB J.* 14:1901-1907) because this protein would initiate negative feedback mechanisms that would be expected to act on both WT and mutant p53.

On the other hand, an independent mechanism favoring mutant accumulation (*e.g.* protection by association with HSP90 (Smith, D, *et al*, 1998, *supra*; Sepehrnia, B, *et al*, 1996, *J. Biol. Chem.* 271:15084-15090) would permit a “recessive” mutant to become in sufficient excess of the transactivating form to result in progressive inhibition of the negative feedback pathways. In this situation, the mutant would have a net DN effect due to progressive accumulation of a stoichiometric antagonist, and selective degradation of that mutant by inhibition of HSP90 activity would be expected to restore normal p53 function. Thus, in most or all cases, a DN phenotype produced by mutant p53 is secondary to the activity of HSP90 and inhibition of HSP90 function with 17-AAG or other HSP90 ATP binding site antagonists would prevent the expression of the DN phenotype and so rescue normal p53 function.

#### **i. Dominant negative p53 mutants**

A list of exemplary p53 mutations, including examples of structurally-abnormal proteins, dominant-negative proteins, prion-like proteins, and mutants with various combinations of these properties, follows:

Chene *et al*, 1999, *Int. J. Cancer*. 82:17-22; Y236delta (deletion of codon 236) resulted in a conformationally altered & dominant-negative phenotype.

Preuss *et al*, 2000, *Int. J. Cancer* 88:162-171); C174Y (Cys→Tyr) (rat) is dominant-negative, non-transactivating. The same mutation at position 176 is predicted to have a similar effect in humans, as the respective homologs have close correlative structural similarities at these positions.

Srivastava *et al*, 1993, *Oncogene* 8:2449-2456); M133T (Met→Thr), G245D (Gly→Asp), and E258K (Glu→Lys) all display conformationally altered, dominant-negative, prion-like displaying activity, in that co-incubation with WT p53 converts it into the mutated conformation.

Deb *et al*, 1999, *Int. J. Oncol.* 15:413-422); 1-293delta (deletion of codons 1-293) exhibited dominant negative DNA binding characteristics without transactivating activity.

Frebourg *et al*, 1992, *Proc. Natl. Acad. Sci.* 89:6413-6417; G245C (Gly→Cys), R248W (Arg→Trp), E258K (Glu→Lys), and R282W (Arg→Try) all independently display conformationally altered, dominant-negative activity.

Brachmann *et al*, 1996, *Proc. Natl. Acad. Sci.* 93:4091-4095; novel yeast assay used to identify dominant-negative p53 mutants that have also been found in human tumors, specifically implicating codons 132, 135, 151, 158, 176, 179, 236, 241, 242, 244, 245, 246, 248, 257, 265, 273, 277, 278, 279, 280, and 281. Of particular interest because they exhibited the greatest dominant-negative activity were mutants at codons 241, 242, 244, 245, 246, 248, 277, 278, 279, 280, and 281.

Blagosklonny *et al*, 1995, *Oncogene* 11:933-939); p53s mutated at the following codons exhibited disrupted conformations were dominant negative, and sensitive to geldanamycin: R175H (Arg→His), 194, 213, 223, 248, 274, R280K (Arg→Lys).

Aurelio *et al*, 2000, *Mol. Cell. Biol.* 20:770-778; without identifying conformational status, the following mutants were identified as dominant-negative for transactivation of apoptotic signals (Bax), but not growth arrest signals (p21<sup>WAF</sup>): V143A (Val→Ala), R175H (Arg→His), G245C (Gly→Cys), R248W (Arg→Trp), R273H (Arg→His), K305M (Lys→Met), G325V (Gly→Val).

Marutani *et al*, 1999, *Cancer Res.* 59:4765-4769; yeast-based transdominance assay used to identify dominant-negative mutations at 16 codons : R156H (Arg→His), R175H (Arg→His), P177S (Pro→Ser), H178P (His→Pro), H179R (His→Arg), R181P (Arg→Pro), 238-9delta (deletion of codons 238 & 239), G245S (Gly→Ser), G245D (Gly→Asp), M246R (Met→Arg),  
 5 R248Q (Arg→Gln), R249S (Arg→Ser), R273H (Arg→His), R273C (Arg→Cys), R273L (Arg→Leu), D281Y (Asp→Tyr).

## ii. Dominant positive p53 mutants

In addition to dominant-negative mutations, some p53 mutations actually transactivate inappropriate gene expression, contributing to oncogenesis; *i.e.* a positive tumor promoting effect.  
 10 See Park *et al*, 1994, *Oncogene* 9:1899-1906. This type of mutation is particularly suited to the approach embodied in the present invention because, unlike in the dominant-negative situation, the presence or absence of a normal allele of the tumor suppressor gene is irrelevant to the therapeutic utility of the HSP90 inhibitor. In other words, because the mutant p53 itself contributes to the malignant process, destruction of the mutant protein by inhibition of HSP90 is  
 15 expected to have direct therapeutic value. A good example is C176Y (Cys→Tyr), as reported by Preuss, U *et al*, 2000, *Int. J. Cancer* 88:162-171. This mutant induces rather than represses the cellular fos promoter, resulting in activation of oncogenic signaling pathways. The biology of “dominant-positive” p53 mutants is reviewed in van Oijen *et al*, 2000, *Clin. Cancer Res.* 6:2138-2145. Other examples of mutations of p53 that give rise to tumorigenic phenotypes include, but  
 20 are not limited to, Phe-132, Val-135, Ala-143, His-175, His-179, Trp-248, Ser-249, Leu-273, His-273 and Gly-281. Of particular interest, because these mutant proteins have been shown to be disrupted conformationally, are Ala-143, His-175, His-179 and Gly-281 (van Oijen, M, *et al*, 2000, *supra*). Particular subsets of the above list of tumor-promoting mutants have been shown to exert their oncogenic effects via transactivation of one or more of the growth promoting genes  
 25 *bFGF*, *IGF-1*, *EGF-R*, and *c-myc*. Alternatively or conjunctively, some gain-of-function mutants, including Ala-143, His-175, Trp-248, Ser-249, His-273, and Gly-281, contribute to tumor resistance to chemotherapeutic drugs by transactivating the *MDR* gene.

As described above, in the case of this type of mutant, in heterozygous cells, selective degradation of that mutant by inhibition of HSP90 activity will restore normal p53 function.  
 30 Furthermore, in cases of loss of heterozygosity (LOH), where the tumor has progressed further and the second, normal p53 allele has become mutated or lost, selective degradation of the

mutated protein by inhibition of HSP90 chaperoning will result in a therapeutic effect. In this case the p53 mutant is behaving as an oncoprotein, as in the bcr-abl and v-src examples described above.

#### **d. Other tumor suppressor variant proteins**

5 In addition to p53 itself, additional members of the p53 family of tumor suppressor proteins have also been implicated in human cancer progression. Although p53 itself is a fairly ubiquitous protein, other family members have more restricted tissue distributions. In particular tissues and tumors derived therefrom, closely related non-p53 proteins serve the same role as p53 itself. In these tumors, a truncated variant, termed deltaN,  
10 predominates over the full-length form. The truncated and/or deletent isoform is able to compete with the full length form for DNA binding, but does not itself have any transactivating activity. Thus, the deltaN form inhibits the tumor suppressor activity of the full length form, so that if the variant is degraded as a result of inhibition of HSP90 activity, an antitumor effect or drug-sensitizing effect will result. The deltaN isoform will  
15 have a heightened dependence on HSP90.

The following three examples concern the specific tumor suppressor proteins p51, p63, and p73. p51 and p63 are each produced from a common 15 exon gene, p73L/p63/p51/p40/KET, and all three proteins exhibit various isoforms, including deltaN isoforms that lack N-terminal transactivation (TA) domains and which are implicated in  
20 various carcinomas treatable according to methods of the invention. The many isotypes possible for these gene products are attributable, at least in part, to complex alternative splicing events and, in the case of p63, multiple promoters. For each, it is understood that isoforms may exist and specific isoform expression patterns may vary as between different tissue types, and as between normal versus carcinomic or neoplastic tissues.

#### **25 i. deltaN p51**

Osada et al. described the cloning and functional analysis of human p51, which structurally and functionally resembles p53. Nature Med. 4: 839-843 (1998). Two major splicing variant gene products have been detected in normal cells, p51A and p51B. p51A (aka TAp63gamma; NCBI #s AB016072 (SEQ ID NOs 280 and 281) is a 448-amino-acid protein with  
30 a molecular weight of 50.9 kDa; and p51B (aka TAp63alpha; AB016073 (SEQ ID NOs 282 and

283) is a 641-amino-acid protein with a molecular weight of 71.9 kDa. Other encoded isoforms have also been observed, including, e.g., those denoted in the following list: p51 delta (NCBI # AF116771 (SEQ ID NOs 284 and 285), delNdelta (NCBI # AAF43493 (SEQ ID NOs 286 and 287), delNbeta (NCBI # AAF43492 (SEQ ID NOs. 288 and 289), delNalpha (NCBI # AAF43491 (SEQ ID NOs. 290 and 291), delNgamma (NCBI # AAF43490; SEQ ID NOs 292 and 293), TAp63delta (NCBI # AAF43489; SEQ ID NOs 294 and 295), TAp63beta (NCBI # AAF43488 (SEQ ID NOs 296 and 297), TAp63alpha (NCBI # AAF43487 (SEQ ID NOs 298 and 299), and TAp63gamma (NCBI # AAF43486 (SEQ ID NOs 300 and 301). The TA isoforms contain a transactivation domain (encoded by exon 3') for transactivating p53; the deltaN forms do not. The absence of the TA domain is thought to render those particular isoforms nonfunctional, thereby contributing to carcinoma etiology at least when those isoforms are expressed in abnormally high amounts. Normal expression patterns of the various isotypes is known to vary as between different tissue types. In lung cancer specimens, for example, multiple deltaN ("TA-less") forms of the p51 protein were found to be overexpressed in 34 of 44 lung cancer specimens analysed (77%). (Tani, M *et al*, 1999, *Neoplasia* 1:71-79).

## ii. deltaN p63

In certain bladder and nasopharyngeal carcinomas, various isoforms of the p53 family member p63 are expressed, and one or more of the deltaN forms, e.g., deltaN p63beta (NCBI # AF075433; SEQ ID NOs 302 and 303), deltaN p63gamma (NCBI # AF075429; SEQ ID NOs 304 and 305), and deltaN p63 alpha (NCBI # AF075431 (SEQ ID NOs 306 and 307) predominate and dominantly inhibit the transactivating activity of the full length TA-containing forms. (Park, B *et al*, 2000, *Cancer Res.* 60:3370-3374). The TA-containing isoforms are TA p63 beta (NCBI # AF075432; SEQ ID NOs 308 and 309) and TA p63 alpha (NCBI # AF075430; SEQ ID NOs 310 and 311). In nasopharyngeal carcinoma, the deltaN isoform predominance is even more pronounced (Crook, T *et al*, 2000, *Oncogene* 19:3439-3444). The p63 protein is also important in UV-B-induced skin cancer. Overexpression of the deltaN isoform of p63 in transgenic mouse epidermis was found to block apoptosis induced by WT p53 in response to UV-B irradiation (Liefer, K, *et al*, 2000, *Cancer Res.* 60:4016-4020). Mutations in the *p63* gene have also been reported in epidermal carcinomas. See, e.g., Osada *et al*, 1998, *Nat. Med.* 4:839-843 and NCBI # NM003722 (SEQ ID NOs 312 and 313).

## iii. deltaN p73

The p73 protein is important in ovarian carcinoma – when compared to primary cultures of normal ovarian epithelial cells, 57% of ovarian carcinoma cell lines, 71% of invasive tumors and 92% of borderline tumor tissues were found to express elevated levels of deltaN p73 (Ng, S *et al*, 2000, *Oncogene* 19:1885-1890). Full-length p73 and isoforms thereof are displayed in NCBI # Y11416 (SEQ ID NOs 314, 315, 316, and 317), along with splice and allelic variations, including splice variations responsible for the deltaN isoform.

Applicants expect that all of the foregoing truncated p53 family members are structurally unstable, dependent on HSP90 and/or exhibit increased sensitivity to HSP90 inhibitors relative to their wild-type counterparts. Applicants further anticipate that other isomeric/aberrant forms of proteins may exhibit similar behavior(s).

The methods of the present invention may be used on mammals, preferably humans, either alone or in combination with other therapies or methods useful for treating a particular cell proliferative disorder or viral infection.

The use of the present invention is facilitated by first identifying whether the cell proliferation disorder or viral infection is accompanied by cells which contain expression of a fusion oncoprotein or a mutated cellular protein with heightened dependence on HSP90 (or a fusion protein or mutant protein that, by one skilled in the art, would be predicted to have heightened dependence on HSP90). Once such disorders are identified, patients suffering from such a disorder can be identified by analysis of their symptoms by procedures well known to medical doctors. Such patients are treated as described herein.

### **3. Representative assays for diagnosing proliferative disorders**

Many different types of methods are known in the art that can be used to diagnose a proliferative disorder characterized by an aberrant protein, *e.g.*, those that involve determining protein concentrations and measuring or predicting the level of proteins within cells, tissues, and fluid samples. Indirect techniques include nucleic acid hybridization and amplification using, *e.g.*, polymerase chain reaction (PCR). These techniques are known to the person of skill and are discussed, *e.g.*, in Sambrook, Fritsch & Maniatis, *Molecular Cloning: A Laboratory Manual*, Second Edition (1989) Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., Ausubel, *et al.*, *Current Protocols in Molecular Biology*, John Wiley & Sons, NY, 1994. Because the nucleic acid sequence is



known, and because the aberrant proteins have a foundational basis in the nucleic acid sequence, the specific sequences found for aberrant proteins can also be used to generate primers and probes that span the novel junction (in the case of fusion proteins), *e.g.*, using RT-PCR and other procedures. For non-fusion proteins, as well as fusion proteins,  
5 stringent hybridization and/or PCR can be used diagnostically.

Polyclonal or monoclonal antibodies can also be generated based on the specific sequence of the aberrant protein (in the case of fusion proteins, preferably the novel amino acid junction itself) using routine techniques. See Harlow *et al.*, *Antibodies: A Laboratory Manual*, 2nd Ed; Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. (1988).

10 Examples of diagnostic methods of that can be used with the invention include those reviewed in Slominski, A *et al*, 1999, *Arch. Pathol. Lab. Med.* 123:1246-1259, O'Connor *et al*, 1999, *Leuk. Lymphoma* 33:53-63, and Scarpa, A *et al*, 1997, *Leuk. Lymphoma* 26 Suppl. 1:77-82. A further list of methods that is intended to be exemplary but not to limit the scope of the invention, follows.

15 O'Connor *et al* , 1997, *Br. J. Haematol.* 99:597-604 described that the t(15;17)(q22;q21) translocation found in APL produces a PML-RAR fusion protein that can be specifically detected with the 5E10 Mab by fluorescence activated cell sorting (FACS).

20 Le *et al* , 1998, *Eur. J. Haematol.* 60:217-225 reported that the AML-ETO fusion protein that arises in t(8;21) AML can be identified in tumor cells with ETO-specific polyclonal antibodies using western blotting. The normal ETO protein (70kD) can be distinguished from the AML-ETO fusion protein (94kD) on the basis of their differing mobilities in the gel.

Viswanatha *et al* , 1998, *Blood* 91:1882-1890 found that the CBFβ-SMMHC fusion protein present in Inv(16)(p13q32) and t(16;16)(p13;q32) AML can be specifically detected with a polyclonal antibody specific for a junctional epitope using FACS of permeabilized cells.

25 In the case of dominantly-acting mutant proteins, such as mutant RET or gain-of-function mutants of p53, the presence of the specific point mutations known to give rise to the dominant mutant may be identified by the molecular genetic techniques listed above in reference to fusion proteins. Numerous reviews of germline and acquired p53 mutations detected in human cancers have been published (*see, e.g.*, Hainuit, P, *et al*, 2000, *Adv. Cancer Res.* 77:81-137).

In the case of dominant-negative p53 mutations, several other diagnostic criteria may be employed to identify patients susceptible of treatment with the current invention. First, molecular genetic methodologies such as Southern Blotting or PCR can be used to detect the presence of a specific point mutation known to give rise to a dominant-negative version of p53. Similarly, FISH  
5 may be employed to detect specific point mutations known to confer conformational changes and/or dominant-negative activity (Villadsen R *et al*, 2000, *Cancer Genet. Cytogenet.* 116:28-34). Other methods include allele-specific PCR (AS-PCR) and chromosome flow cytometry (Villadsen *et al*, *Supra*).

Alternatively, if the mutation in question has not previously been shown to generate a  
10 dominant-negative p53 mutant, a cell-based transdominance assay may be used to determine the phenotype (Frebourg, T *et al*, 1992, *Proc. Natl. Acad. Sci.* 89:6413-6417). In this assay, p53-null SAOS-2 cells are co-transfected with WT p53 and the test mutant. The normal p53 protein causes the cells to undergo apoptosis, from which fate they can be rescued by a p53 mutant that has a dominant negative activity. In these cases, further genetic analyses may be performed to confirm  
15 the presence of an intact non-mutant allele. In addition, antibodies have been raised that distinguish between p53 proteins with normal versus mutant conformation. These latter p53s have a heightened dependence upon HSP90, and so fall within the scope of the present invention. Specifically, PAb240, from (Oncogene Sciences, Inc.) OSI, is mutant conformation-specific. The corresponding antibody specific for WT is PAb1620, also for OSI (Chene, P, *et al*, 1999, *supra*).

In the case of cell proliferative disorders arising due to unwanted proliferation of non-cancer cells, the level of the fusion protein or mutated cellular protein is compared to that level occurring in the general population (*e.g.*, the average level occurring in the general population of people or animals excluding those people or animals suffering from a cell proliferative disorder). If the unwanted cell proliferation disorder is characterized by an abnormal level of a fusion  
20 protein than occurs in a normal population, or by the presence of a mutated cellular protein, such as p53, then the disorder is a candidate for treatment using the methods described herein. In a preferred example, the mutated protein is p53 and the proliferative disorder is rheumatoid arthritis. In a particularly preferred example, the p53 mutations may include, but are not limited to, N239S (Asn→Ser), C176R (Cys-Arg) and R213\* (Arg→stop) and the mutant forms exert  
25 apparent dominant-negative activity over the wild-type protein. (Han, Z *et al*, 1999, *Arthritis Rheum.* 42:1088-1092).  
30

#### 4. Preparation and Administration of Pharmaceutical Compositions

Geldanamycin may be prepared according to U.S. Patent No. 3,595,955 using the subculture of *Streptomyces hygroscopicus* that is on deposit with the U.S. Department of Agriculture, Northern Utilization and Research Division, Agricultural Research, Peoria, Ill., USA, accession number NRRL 3602. It is also available from Sigma/Aldrich Chemical Co., St. Louis, Mo., USA. Numerous derivatives of this compound, including herbimycin A, macbecin, and 17-AAG may be fashioned as specified in U.S. Patent Nos. 4, 261, 989, 5,387,584, and 5,932,566, or according to standard techniques known in the art. Other useful ansamycin derivatives appear in Applicants' co-pending and commonly owned provisional application entitled, "*Ansamycins Having Improved Pharmacological and Biological Properties*," filed February 8, 2002, Serial Number to be determined, and herein incorporated by reference in its entirety.

Those of ordinary skill in the art are familiar with formulation and administration techniques that can be employed in use of the invention, *e.g.*, as discussed in Goodman and Gilman's *The Pharmacological Basis of Therapeutics*, current edition; Pergamon Press; and Remington's *Pharmaceutical Sciences* (current edition.) Mack Publishing Co., Easton, Pa.

The compounds utilized in the methods of the instant invention may be administered either alone or in combination with pharmaceutically acceptable carriers, excipients or diluents, in a pharmaceutical composition, according to standard pharmaceutical practice. The compounds can be administered orally or parenterally, including the intravenous, intramuscular, intraperitoneal, subcutaneous, rectal and topical routes of administration.

The pharmaceutical compositions used in the methods of the instant invention can contain the active ingredient in a form suitable for oral use, for example, as tablets, troches, lozenges, aqueous or oily suspensions, dispersible powders or granules, emulsions, hard or soft capsules, or syrups or elixirs. Compositions intended for oral use may be prepared according to any method known to the art for the manufacture of pharmaceutical compositions and such compositions may contain one or more agents selected from the group consisting of sweetening agents, flavoring agents, coloring agents and preserving agents in order to provide pharmaceutically elegant and palatable preparations. Tablets contain the active ingredient in admixture with non-toxic pharmaceutically acceptable excipients which are suitable for the manufacture of tablets. These excipients may be, for example, inert diluents, such as calcium carbonate, sodium carbonate,

lactose, calcium phosphate or sodium phosphate; granulating and disintegrating agents, such as microcrystalline cellulose, sodium crosscarmellose, corn starch, or alginic acid; binding agents, for example starch, gelatin, polyvinyl-pyrrolidone or acacia, and lubricating agents, for example, magnesium stearate, stearic acid or talc. The tablets may be uncoated or they may be coated by known techniques to mask the unpleasant taste of the drug or delay disintegration and absorption in the gastrointestinal tract and thereby provide a sustained action over a longer period. For example, a water soluble taste masking material such as hydroxypropylmethyl-cellulose or hydroxypropylcellulose, or a time delay material such as ethyl cellulose, cellulose acetate butyrate may be employed.

Formulations for oral use may also be presented as hard gelatin capsules wherein the active ingredient is mixed with an inert solid diluent, for example, calcium carbonate, calcium phosphate or kaolin, or as soft gelatin capsules wherein the active ingredient is mixed with water soluble carrier such as polyethyleneglycol or an oil medium, for example peanut oil, liquid paraffin, or olive oil.

Aqueous suspensions contain the active material in admixture with excipients suitable for the manufacture of aqueous suspensions. Such excipients are suspending agents, for example sodium carboxymethylcellulose, methylcellulose, hydroxypropylmethyl-cellulose, sodium alginate, polyvinyl-pyrrolidone, gum tragacanth and gum acacia; dispersing or wetting agents may be a naturally-occurring phosphatide, for example lecithin, or condensation products of an alkylene oxide with fatty acids, for example polyoxyethylene stearate, or condensation products of ethylene oxide with long chain aliphatic alcohols, for example heptadecaethylene-oxycetanol, or condensation products of ethylene oxide with partial esters derived from fatty acids and a hexitol such as polyoxyethylene sorbitol monooleate, or condensation products of ethylene oxide with partial esters derived from fatty acids and hexitol anhydrides, for example polyethylene sorbitan monooleate. The aqueous suspensions may also contain one or more preservatives, for example ethyl, or n-propyl p-hydroxybenzoate, one or more coloring agents, one or more flavoring agents, and one or more sweetening agents, such as sucrose, saccharin or aspartame.

Oily suspensions may be formulated by suspending the active ingredient in a vegetable oil, for example arachis oil, olive oil, sesame oil or coconut oil, or in mineral oil such as liquid paraffin. The oily suspensions may contain a thickening agent, for example beeswax, hard paraffin or cetyl alcohol. Sweetening agents such as those set forth above, and flavoring agents

may be added to provide a palatable oral preparation. These compositions may be preserved by the addition of an anti-oxidant such as butylated hydroxyanisol or alpha-tocopherol.

Dispersible powders and granules suitable for preparation of an aqueous suspension by the addition of water provide the active ingredient in admixture with a dispersing or wetting agent, suspending agent and one or more preservatives. Suitable dispersing or wetting agents and suspending agents are exemplified by those already mentioned above. Additional excipients, for example sweetening, flavoring and coloring agents, may also be present. These compositions may be preserved by the addition of an anti-oxidant such as ascorbic acid.

The pharmaceutical compositions used in the methods of the instant invention may also be in the form of oil-in-water emulsions. The oily phase may be a vegetable oil, for example olive oil or arachis oil, or a mineral oil, for example liquid paraffin or mixtures of these. Suitable emulsifying agents may be naturally-occurring phosphatides, for example soy bean lecithin, and esters or partial esters derived from fatty acids and hexitol anhydrides, for example sorbitan monooleate, and condensation products of the said partial esters with ethylene oxide, for example polyoxyethylene sorbitan monooleate. The emulsions may also contain sweetening, flavoring agents, preservatives and antioxidants.

Syrups and elixirs may be formulated with sweetening agents, for example glycerol, propylene glycol, sorbitol or sucrose. Such formulations may also contain a demulcent, a preservative, flavoring and coloring agents and antioxidant.

The pharmaceutical compositions may be in the form of sterile injectable aqueous solutions. Among the acceptable vehicles and solvents that may be employed are water, Ringer's solution and isotonic sodium chloride solution.

The sterile injectable preparation may also be a sterile injectable oil-in-water microemulsion where the active ingredient is dissolved in the oily phase. For example, the active ingredient may be first dissolved in a mixture of soybean oil and lecithin. The oil solution then introduced into a water and glycerol mixture and processed to form a microemulsion.

The injectable solutions or microemulsions may be introduced into a patient's blood-stream by local bolus injection. Alternatively, it may be advantageous to administer the solution or microemulsion in such a way as to maintain a constant circulating concentration of the instant

compound. In order to maintain such a constant concentration, a continuous intravenous delivery device may be utilized. An example of such a device is the Deltec CADD-PLUS™ model 5400 intravenous pump.

The pharmaceutical compositions may be in the form of a sterile injectable aqueous or oleagenous suspension for intramuscular and subcutaneous administration. This suspension may be formulated according to the known art using those suitable dispersing or wetting agents and suspending agents which have been mentioned above. The sterile injectable preparation may also be a sterile injectable solution or suspension in a non-toxic parenterally-acceptable diluent or solvent, for example as a solution in 1,3-butane diol. In addition, sterile, fixed oils are conventionally employed as a solvent or suspending medium. For this purpose any bland fixed oil may be employed including mono- or diglycerides. In addition, fatty acids such as oleic acid find use in the preparation of injectables.

The HSP90 inhibitors used in the methods of the present invention may also be administered in the form of a suppositories for rectal administration of the drug. These compositions can be prepared by mixing the inhibitors with a suitable non-irritating excipient which is solid at ordinary temperatures but liquid at the rectal temperature and will therefore melt in the rectum to release the drug. Such materials include cocoa butter, glycerinated gelatin, hydrogenated vegetable oils, mixtures of polyethylene glycols of various molecular weights and fatty acid esters of polyethylene glycol.

For topical use, creams, ointments, jellies, solutions or suspensions, etc., containing an HSP90 inhibitor can be used. (As used herein, topical application can include mouth washes and gargles.)

The compounds used in the methods of the present invention can be administered in intranasal form via topical use of suitable intranasal vehicles and delivery devices, or via transdermal routes, using those forms of transdermal skin patches well known to those of ordinary skill in the art. To be administered in the form of a transdermal delivery system, the dosage administration will, of course, be continuous rather than intermittent throughout the dosage regimen.

The HSP90 inhibitors used in the instant invention may also be co-administered with other well known therapeutic agents that are selected for their particular usefulness against the

condition that is being treated. For example, the instant compounds may be useful in combination with known anti-cancer and cytotoxic agents. The instant compounds may also be useful in combination with other inhibitors of parts of the signaling pathway that links cell surface growth factor receptors to nuclear signals initiating cellular proliferation.

5           The methods of the present invention may also be useful with other agents that inhibit angiogenesis and thereby inhibit the growth and invasiveness of tumor cells, including, but not limited to VEGF receptor inhibitors, angiostatin and endostatin.

          When a HSP90 inhibitor used in the methods of the present invention is administered into a human subject, the daily dosage will normally be determined by the prescribing physician with  
10   the dosage generally varying according to the age, weight, and response of the individual patient, as well as the severity of the patient's symptoms.

          In one exemplary application, a suitable amount of a HSP90 inhibitor is administered to a mammal undergoing treatment for cancer. Administration occurs in an amount of each type of inhibitor of between about 0.1 mg/kg of body weight to about 60 mg/kg of body weight per day,  
15   preferably of between 0.5 mg/kg of body weight to about 40 mg/kg of body weight per day. A particular therapeutic dosage that comprises the instant composition includes from about 0.01 mg to about 1000 mg of a HSP90 inhibitor. Preferably, the dosage comprises from about 1 mg to about 1000 mg of a HSP90 inhibitor.

          Examples of antineoplastic agents which can be used in combination with the methods of  
20   the present invention include, in general, alkylating agents, anti-metabolites; epidophyllotoxin; an antineoplastic enzyme; a topoisomerase inhibitor; procarbazine; mitoxantrone; platinum coordination complexes; biological response modifiers and growth inhibitors; hormonal/anti-hormonal therapeutic agents and haematopoietic growth factors.

          Exemplary classes of antineoplastic agents further include the anthracycline family of  
25   drugs, the vinca drugs, the mitomycins, the bleomycins, the cytotoxic nucleosides, the epothilones, discodermolide, the pteridine family of drugs, diynenes and the podophyllotoxins. Particularly useful members of those classes include, for example, carminomycin, daunorubicin, aminopterin, methotrexate, methopterin, dichloromethotrexate, mitomycin C, porfiromycin, 5-fluorouracil, 6-mercaptopurine, gemcitabine, cytosine arabinoside, podophyllotoxin or podo-  
30   phyllotoxin derivatives such as etoposide, etoposide phosphate or teniposide, melphalan,

vinblastine, vincristine, leurosidine, vindesine, leurosine, paclitaxel and the like. Other useful antineoplastic agents include estramustine, carboplatin, cyclophosphamide, bleomycin, gemcitabine, ifosamide, melphalan, hexamethyl melamine, thiotepa, cytarabin, idatrexate, trimetrexate, dacarbazine, L-asparaginase, camptothecin, CPT-11, topotecan, ara-C, bicalutamide, 5 flutamide, leuprolide, pyridobenzoindole derivatives, interferons and interleukins.

Preferably, the pharmaceutical preparation is in unit dosage form. In such form, the preparation is subdivided into unit doses containing appropriate quantities of the active component, *e.g.*, an effective amount to achieve the desired purpose.

10 The quantity of active compound in a unit dose of preparation may be varied or adjusted from about 0.1 mg to 1000 mg, preferably from about 1 mg to 300 mg, more preferably 10 mg to 200 mg, according to the particular application.

The actual dosage employed may be varied depending upon the requirements of the patient and the severity of the condition being treated. Determination of the proper dosage for a particular situation is within the skill of the art. Generally, treatment is initiated with smaller 15 dosages which are less than the optimum dose of the compound. Thereafter, the dosage is increased by small amounts until the optimum effect under the circumstances is reached. For convenience, the total daily dosage may be divided and administered in portions during the day if desired.

The amount and frequency of administration of the HSP90 inhibitors used in the methods 20 of the present invention and, if applicable, other chemotherapeutic agents and/or radiation therapy will be regulated according to the judgment of the attending clinician (physician) considering such factors as age, condition and size of the patient as well as severity of the disease being treated. A dosage regimen of the HSP90 inhibitors can be intravenous administration of from 1 mg to 5gm/day, more preferably 10 mg to 2000 mg/day, more preferably still 10 to 1000 mg/day, and 25 most preferably 50 to 600 mg/day, in one or more (preferably two) doses, to block tumor growth.

The chemotherapeutic agent and/or radiation therapy can be administered according to therapeutic protocols well known in the art. It will be apparent to those skilled in the art that the administration of the chemotherapeutic agent and/or radiation therapy can be varied depending on the disease being treated and the known effects of the chemotherapeutic agent and/or radiation 30 therapy on that disease. Also, in accordance with the knowledge of the skilled clinician, the



therapeutic protocols (*e.g.*, dosage amounts and times of administration) can be varied in view of the observed effects of the administered therapeutic agents (*i.e.*, antineoplastic agent or radiation) on the patient, and in view of the observed responses of the disease to the administered therapeutic agents.

5           Also, in general, the HSP90 inhibitor and the chemotherapeutic agent do not have to be administered in the same pharmaceutical composition, and may, because of different physical and chemical characteristics, have to be administered by different routes. For example, the HSP90 inhibitor may be administered orally to generate and maintain good blood levels, while the chemotherapeutic agent may be administered intravenously. The determination of the mode of  
10       administration and the advisability of administration, where possible, in the same pharmaceutical composition, is well within the knowledge of the skilled clinician. The initial administration can be made according to established protocols known in the art, and then, based upon the observed effects, the dosage, modes of administration and times of administration can be modified by the skilled clinician.

15           The particular choice of HSP90 inhibitor, and chemotherapeutic agent and/or radiation will depend upon the diagnosis of the attending physicians and their judgment of the condition of the patient and the appropriate treatment protocol.

          The HSP90 inhibitor, and chemotherapeutic agent and/or radiation may be administered concurrently (*e.g.*, simultaneously, essentially simultaneously or within the same treatment  
20       protocol) or sequentially, depending upon the nature of the proliferative disease, the condition of the patient, and the actual choice of chemotherapeutic agent and/or radiation to be administered in conjunction (*i.e.*, within a single treatment protocol) with the HSP90 inhibitor.

          If the HSP90 inhibitor, and the chemotherapeutic agent and/or radiation are not administered simultaneously or essentially simultaneously, then the optimum order of  
25       administration of the HSP90 inhibitor, and the chemotherapeutic agent and/or radiation, may be different for different tumors. Thus, in certain situations the HSP90 inhibitor may be administered first followed by the administration of the chemotherapeutic agent and/or radiation; and in other situations the chemotherapeutic agent and/or radiation may be administered first followed by the administration of the HSP90 inhibitor. This alternate administration may be  
30       repeated during a single treatment protocol. The determination of the order of administration, and the number of repetitions of administration of each therapeutic agent during a treatment protocol,

is well within the knowledge of the skilled physician after evaluation of the disease being treated and the condition of the patient. For example, the chemotherapeutic agent and/or radiation may be administered first, especially if it is a cytotoxic agent, and then the treatment continued with the administration of the HSP90 inhibitor followed, where determined advantageous, by the administration of the chemotherapeutic agent and/or radiation, and so on until the treatment protocol is complete.

Thus, in accordance with experience and knowledge, the practicing physician can modify each protocol for the administration of a component (therapeutic agent-*i.e.*, HSP90 inhibitor, chemotherapeutic agent or radiation) of the treatment according to the individual patient's needs, as the treatment proceeds.

The attending clinician, in judging whether treatment is effective at the dosage administered, will consider the general well-being of the patient as well as more definite signs such as relief of disease-related symptoms, inhibition of tumor growth, actual shrinkage of the tumor, or inhibition of metastasis. Size of the tumor can be measured by standard methods such as radiological studies, *e.g.*, CAT or MRI scan, and successive measurements can be used to judge whether or not growth of the tumor has been retarded or even reversed. Relief of disease-related symptoms such as pain, and improvement in overall condition can also be used to help judge effectiveness of treatment.

## EXAMPLES

The following examples are illustrative only, and are not intended to be limiting of the invention.

### Example 1:

#### Cytotoxic Activity of 17AAG on K562 Versus a Normal Cell Type

Grosveld et al., Mol Cell Biol 6(2):607-16 (1986) showed that the chronic myelocytic cell line K562 produces a chimeric bcr/c-abl transcript, making it a suitable model system to demonstrate the methods of the invention. The cell line is widely available, *e.g.*, from American Type Culture Collection ("ATCC"; Manassas, VA, USA; cat# CCL-243) and can be propagated in a variety of media, *e.g.*, ATCC's Iscove's modified Dulbecco's medium with 4 mM L-glutamine adjusted to contain 1.5 g/L sodium bicarbonate, 90%; fetal bovine serum, 10%; 37C.

### *Experimental*

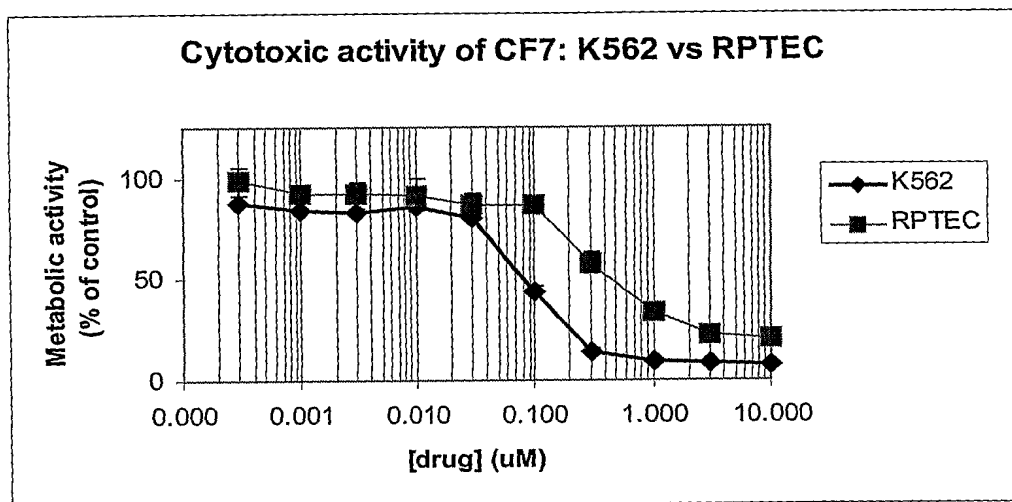
To K562 cells (suspension grown in DMEM media supplemented w/10% Fetal Bovine Serum (FBS) and 1mM HEPES; subcultured biweekly at 100K cells/ml) in a 96 well plate (0.1 ml medium; 2000 cells per well) were added various concentrations of 17-AAG (CF7) and the effects measured over a period of 3-6 days using an MTS assay protocol similar to that offered by Promega Corp (Madison, WI, US; cat# G5421).

The MTS assay is a colorimetric assay for determining the number of viable cells in proliferation, cytotoxicity or chemosensitivity assays. The CellTiter 96® AQueous Assay is composed of solutions of tetrazolium compound (3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H- tetrazolium, inner salt; MTS) and an electron coupling reagent (phenazine methosulfate) PMS. MTS is bio-reduced by cells into a formazan that is soluble in tissue culture medium. Barltrop et al. (1991) Bioorg. & Med. Chem. Lett. 1, 611. The absorbance of the formazan at 490nm can be measured directly from 96 well assay plates without additional processing. Cory et al. (1991) Cancer Commun. 3, 207; Riss, T.L. and Moravec, R.A. (1992) Mol. Biol. Cell 3 (Suppl.), 184a. The conversion of MTS into the aqueous soluble formazan is accomplished by dehydrogenase enzymes found in metabolically active cells. The quantity of formazan product as measured by the amount of 490nm absorbance is directly proportional to the number of living cells in culture.

Using the MTS assay, cytotoxicity (defined as “growth inhibition” and not necessarily versus renal proximal tubular endothelial cells (normal cells) was determined as shown in the following Tables. “Sem” refers to standard error of the mean, which is calculated as the standard deviation divided by the square root of the sample size; the numbers reflect triplicate replicates. Dilutions of the compounds were prepared in DMSO and straight DMSO was used as a control corresponding to 100% metabolic activity.

Conc (uM)	Metabolic Activity			
	K562	sem1	RPTEC	sem1
10.0000	7.89	0.56	20.10	2.64
3.0000	8.12	1.02	22.01	2.49
1.0000	9.51	0.59	34.01	0.19
0.3000	14.40	1.53	58.03	5.09
0.1000	44.06	2.76	86.46	1.51
0.0300	80.12	2.29	86.40	5.96
0.0100	85.94	0.06	91.81	8.22
0.0030	83.00	2.25	92.73	4.79

0.0010	83.81	0.73	92.26	2.97
0.0003	88.00	0.40	98.69	7.16

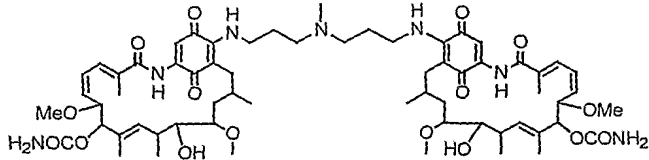
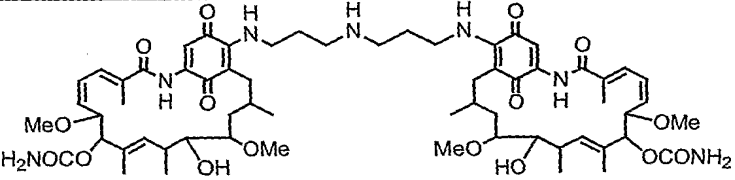
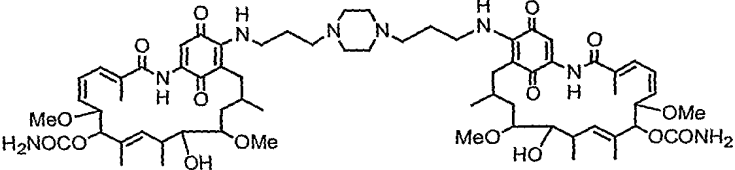
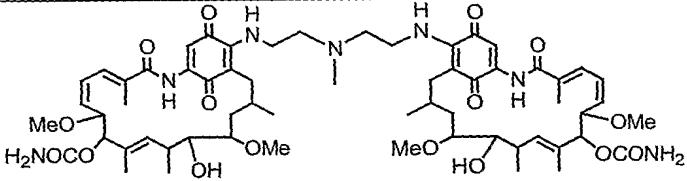
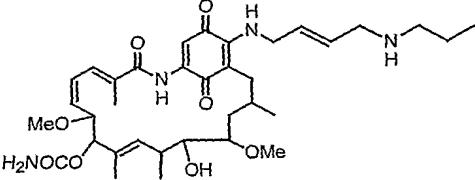


As demonstrated, the fusion protein cancer line K562 is more sensitive to the HSP90 inhibitor than is the normal cell line, RPTEC. It is expected that this will hold true for a variety of tumor cell lines versus a variety of normal cell lines.

In addition to the effects of 17-AAG on K562 versus RPTEC, the effects of a number of other putative HSP90 inhibitors and control compounds were tested side-by-side per the following Table, where "NEC" refers to no effective concentration.

Compound	RPTEC IC <sub>50</sub> (nM)	K562 IC <sub>50</sub> (nM)
CF7	400	70
DMSO	NEC	NEC
208	1000	50
237	4000	100
483	1000	70
481	4000	400

In the table, compound CF7 is the well known 17-AAG and compounds 207, 208, 237, 483, and 481 have the following formulas.

Compound #	Formula
208	 <p>a water soluble dimer</p>
237	 <p>a water soluble dimer</p>
207	 <p>a water soluble dimer</p>
483	 <p>a water soluble dimer</p>
481	 <p>a water soluble prodrug</p>

A separate study using the well known compound, radicicol, yielded results approximating those obtained for compound 237. Preparation of compounds 207, 208, 237, 483, and 481 is described in the following examples.

### Example 2:

#### Preparation of Compound #208

3,3'-diamino-N-methyldipropylamine (1.32g, 9.1mmol) was added dropwise to a solution of Geldanamycin (10g, 17.83mmol) in DMSO (200ml) in a flame-dried flask under N<sub>2</sub> and stirred at room temperature. The reaction mixture was diluted with water after 12 hours. A precipitate was formed and filtered to give the crude product. The crude product was chromatographed by silica chromatography (5% CH<sub>3</sub>OH/CH<sub>2</sub>Cl<sub>2</sub>) to afford the desired dimer as a purple solid (8.92g, 7.2mmol). Yield: 81%; mp 153°C (dec.); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  0.95 (d, J = 7 Hz, 6H, 2CH<sub>3</sub>), 1.0 (d, J = 7 Hz, 6H, 2CH<sub>3</sub>), 1.69 (m, 4 H, 2 CH<sub>2</sub>), 1.74 (m, 4 H, 2CH<sub>2</sub>), 1.76 (s, 6 H, 2 CH<sub>3</sub>), 1.83 (m, 2H, 2CH), 2.0 (s, 6H, 2CH<sub>3</sub>), 2.3 (s, 3H, N-CH<sub>3</sub>), 2.36(dd, J = 14Hz, 2H, 2CH), 2.5 (m, 4H, 2CH<sub>2</sub>), 2.63 (d, 2H, 2CH), 2.75(m, 2H, 2CH), 3.25(s, 6H, 2OCH<sub>3</sub>), 3.35(s, 6H, 2OCH<sub>3</sub>), 3.4 (m, 2H, 2CH), 3.50 (m, 4H, 2CH<sub>2</sub>), 3.68(m, 2H, 2CH), 4.2(Bs, 2H, OH), 4.3( d, J = 10 Hz, 2H, 2CH), 4.8(Bs, 4H, 2NH<sub>2</sub>), 5.19(s, 2H, 2CH), 5.82(t, J = 15 Hz, 2H, 2CH=), 5.89(d, J = 10 Hz, 2H, 2CH=), 6.59( t, J = 15 Hz, 2H, 2CH=), 6.92 (d, J = 10 Hz, 2H, 2CH=), 7.13 (t, 2H, 2NH ), 7.24(s, 2H, 2CH=), 9.21(s, 2H, 2NH); MS (m/z)1203 (M+H).

The corresponding HCl salt was prepared by the following method: an HCl solution in EtOH (5 ml, 0.123N) was added to a solution of compound #208 (1 gm as prepared above) in THF (15 ml) and EtOH (50 ml) at room temperature. The reaction mixture was stirred for 10 min. The salt was precipitated, filtered and washed with large amount of EtOH and dried in vacuo.

### Example 3:

#### Preparation of Compound #207

Compound #207 was prepared by the same method described in example 2 except that 1,4-bis (3-aminopropyl) piperazine was used instead of 3,3'-diamino-N-methyldipropylamine. The pure purple product was obtained after column chromatography (silica gel); yield: 90%; mp 162°C; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  0.97 (d, J = 6.6 Hz, 6H, 2CH<sub>3</sub>), 1.0 (d, J = 6.6 Hz, 6H, 2CH<sub>3</sub>), 1.73 (m, 4 H, 2 CH<sub>2</sub>), 1.78 (m, 4 H, 2CH<sub>2</sub>), 1.80 (s, 6 H, 2 CH<sub>3</sub>), 1.85 (m, 2H, 2CH), 2.0 (s, 6H, 2CH<sub>3</sub>), 2.4 (dd, J = 11Hz, 2H, 2CH), 2.55 (m, 8H, 4CH<sub>2</sub>), 2.67 (d, J = 15 Hz, 2H, 2CH), 2.63 (t, J = 10 HZ, 2H, 2CH), 2.78(t, J = 6.5 Hz, 4H, 2CH<sub>2</sub>), 3.26(s, 6H, 2OCH<sub>3</sub>), 3.38(s, 6H, 2OCH<sub>3</sub>), 3.4 (m, 2H, 2CH), 3.60 (m, 4H, 2CH<sub>2</sub>), 3.75(m, 2H, 2CH), 4.6( d, J = 10 Hz, 2H, 2CH), 4.65 (Bs, 2H, 2OH), 4.8(Bs, 4H, 2NH<sub>2</sub>), 5.19(s, 2H, CH), 5.83(t, J = 15 Hz, 2H, 2CH=), 5.89(d, J = 10 Hz, 2H, 2CH=), 6.58( t, J = 15 Hz, 2H, 2CH=), 6.94 (d, J = 10 Hz, 2H, 2CH=), 7.24(s, 2H, 2CH=), 7.60 (m, 2H, 2NH), 9.20(s, 2H, 2NH); MS (m/z) 1258 (M+H); The corresponding HCl salt was prepared by the same procedure as described in example 1.

**Example 4:****Preparation of Compound #237**

Compound #237 was prepared by the same method described in example 2 except that 3,3'-diamino-dipropylamine was used instead of 3,3'-diamino-N-methyldipropylamine. The pure purple product was obtained after flash chromatography (silica gel); yield: 93%; mp 165°C; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  0.97 (d, J = 6.6 Hz, 6H, 2CH<sub>3</sub>), 1.0 (d, J = 6.6 Hz, 6H, 2CH<sub>3</sub>), 1.72 (m, 4 H, 2 CH<sub>2</sub>), 1.78 (m, 4 H, 2CH<sub>2</sub>), 1.80 (s, 6 H, 2 CH<sub>3</sub>), 1.85 (m, 2H, 2CH), 2.0 (s, 6H, 2CH<sub>3</sub>), 2.4 (dd, J = 11Hz, 2H, 2CH), 2.67 (d, J = 15 Hz, 2H, 2CH), 2.63 (t, J = 10 HZ, 2H, 2CH), 2.78(t, J = 6.5 Hz, 4H, 2CH<sub>2</sub>), 3.26(s, 6H, 2OCH<sub>3</sub>), 3.38(s, 6H, 2OCH<sub>3</sub>), 3.4 (m, 2H, 2CH), 3.60 (m, 4H, 2CH<sub>2</sub>), 3.75(m, 2H, 2CH), 4.6( d, J = 10 Hz, 2H, 2CH), 4.65 (Bs, 2H, 2OH), 4.8(Bs, 4H, 2NH<sub>2</sub>), 5.19(s, 2H, 2CH), 5.83(t, J = 15 Hz, 2H, 2CH=), 5.89(d, J = 10 Hz, 2H, 2CH=), 6.58( t, J = 15 Hz, 2H, 2CH=), 6.94 (d, J = 10 Hz, 2H, 2CH=), 7.17 (m, 2H, 2NH ), 7.24(s, 2H, 2CH=), 9.20(s, 2H, 2NH); MS (m/z)1189 (M+H); The corresponding HCl salt was prepared by the same procedure as described in example 1.

**Example 5:****Preparation of Compound #483**

Compound #483 was prepared by the same method described in example 2 except that 2,2'-diamino-N-methyldiethylamine was used instead of 3,3'-diamino-N-methyldipropylamine. The pure purple product was obtained after flash chromatography; yield: 90%; mp 167-169 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  0.95 (d, J = 7 Hz, 6H, 2CH<sub>3</sub>), 1.00 (d, J = 7 Hz, 6H, 2CH<sub>3</sub>), 1.85 (m, 4 H, 2CH<sub>2</sub>), 1.75 (s, 6 H, 2 CH<sub>3</sub>), 1.80 (m, 2H, 2CH), 2.0 (s, 6H, 2CH<sub>3</sub>), 2.30 (s, 3H, N-CH<sub>3</sub>), 2.30 (dd, J = 14Hz, 2H, 2CH), 2.5 (m, 4H, 2CH<sub>2</sub>), 2.63 (d, 2H, 2CH), 2.75(m, 2H, 2CH), 3.25(s, 6H, 2OCH<sub>3</sub>), 3.35(s, 6H, 2OCH<sub>3</sub>), 3.4 (m, 2H, 2CH), 3.50 (m, 4H, 2CH<sub>2</sub>), 3.68(m, 2H, 2CH), 4.2(Bs, 2H, OH), 4.30 (d, J = 10 Hz, 2H, 2CH), 4.8(Bs, 4H, 2NH<sub>2</sub>), 5.19 (s, 2H, 2CH), 5.82 (t, J = 15 Hz, 2H, 2CH=), 5.90 (d, J = 10 Hz, 2H, 2CH=), 6.59( t, J = 15 Hz, 2H, 2CH=), 6.92 (d, J = 10 Hz, 2H, 2CH=), 7.13 (t, 2H, 2NH ), 7.24 (s, 2H, 2CH=), 9.20 (s, 2H, 2NH); MS (m/z)1175 (M+H); ); The corresponding HCl salt was prepared by the same procedure as described in example 1.

**Example 6:****Preparation of Compound #481**

To 200 mg (0.357 mmol) of geldanamycin in 8 ml of dry THF in a flame-dried flask was added 91.6 mg (0.714 mmol) of N-propyl-1,4-diamino-2-butene drop-wise under nitrogen. The reaction mixture was stirred at room temperature for 4 h at which time TLC analysis indicated the reaction was complete. The solvent was removed by rotary evaporation and the crude material was chromatographed (5% CH<sub>3</sub>OH/CH<sub>2</sub>Cl<sub>2</sub> to 15% CH<sub>3</sub>OH/CH<sub>2</sub>Cl<sub>2</sub>) to afford the desired compound as a purple solid (150 mg, 0.228 mmol); yield: 64%; mp 131°C; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  0.97 (m, 9H, 3CH<sub>3</sub>), 1.52 (m, 2H, CH<sub>2</sub>), 1.72 (m, 3H, CH + CH<sub>2</sub>), 1.80 (s, 3H, CH<sub>3</sub>), 2.0 (s, 3H, CH<sub>3</sub>), 2.38 (dd, J = 11 Hz, 1H, CH), 2.72 (m, 4H, 2CH, CH<sub>2</sub>), 3.26 (s, 3H, OCH<sub>3</sub>), 3.38 (s, 3H, OCH<sub>3</sub>), 3.46 (m, H, CH), 3.6 (m, H, CH), 4.18 (m, 4H, 2CH<sub>2</sub>), 4.34 (d, J = 10 Hz, 1H, CH), 4.8 (Bs, 2H, NH<sub>2</sub>), 5.19 (s, 1H, CH), 5.88 (m, 4H, 4CH=), 6.38 (m, 1H, NH), 6.61 (t, J = 15 Hz, 1H, CH=), 6.94 (d, J = 10 Hz, 1H, CH=), 7.30 (s, H, CH=), 9.16 (s, H, NH); MS (m/z) 658 (M+H). The corresponding HCl salt was prepared by the same procedure as described in example 1.

\* \* \*

Various patents, publications, and formulations are within the levels of ordinary skill in the art to which the invention pertains. All documents including the sequence listing cited in this disclosure are incorporated by reference to the same extent as if each reference had been incorporated by reference in its entirety individually, although none is admitted to be prior art.

One skilled in the art would readily appreciate that the present invention is well adapted to carry out the objects and obtain the ends and advantages mentioned, as well as those inherent therein. The methods and compositions described herein as presently representative of preferred embodiments are exemplary and are not intended as limitations on the scope of the invention. Changes therein and other uses will occur to those skilled in the art, are encompassed within the spirit of the invention, and are defined by the scope of the claims.

It will be readily apparent to one skilled in the art that varying substitutions and modifications may be made to the invention disclosed herein without departing from the scope and spirit of the invention. Thus, such additional embodiments are within the scope of the present invention and the following claims.



The invention illustratively described herein suitably may be practiced in the absence of any element or elements, limitation or limitations which is not specifically disclosed herein. Thus, for example, in each instance herein any of the terms “comprising,” “consisting essentially of” and “consisting of” may be replaced with either of the other two terms. The terms and expressions  
5 which have been employed are used as terms of description and not of limitation, and there is no intention that in the use of such terms and expressions of excluding any equivalents of the features shown and described or portions thereof, but it is recognized that various modifications are possible within the scope of the invention claimed. Thus, it should be understood that although the present invention has been specifically disclosed by preferred embodiments, optional features,  
10 modification and variation of the concepts herein disclosed may be resorted to by those skilled in the art, and that such modifications and variations are considered to be within the scope of this invention as defined by the description and the appended claims.

In addition, where features or aspects of the invention are described in terms of Markush groups or other grouping of alternatives, those skilled in the art will recognize that the invention is  
15 also thereby described in terms of any individual member or subgroup of members of the Markush group or other group, and exclusions of individual members as appropriate.

## Claims

We claim:

1. A method of treating a patient having a genetically-defined disease characterized by a chromosomal aberration that yields an oncogenic fusion protein, comprising:
  - 5 providing a cell, tissue, or fluid sample of a patient suspected of having said genetically-defined disease;
  - identifying one or more characteristics indicative of said disease in or on said cell, tissue, or fluid sample; and
  - administering to said patient a pharmaceutically effective amount of an HSP90-  
10 inhibiting compound.
2. The method of claim 1, wherein said compound is an ansamycin.
3. The method of claim 2, wherein said ansamycin is selected from the group consisting of geldanamycin, 17-AAG, herbimycin A, and macbecin.
4. The method of claim 2, wherein said ansamycin is 17-AAG.
- 15 5. The method of claim 1, wherein said compound is a compound that binds into the ATP-binding site of a HSP90.
- 6 The method of claim 5 wherein said compound is radicicol or an analog thereof.
7. The method of claim 1 wherein said identifying comprises using PCR or LCR to identify a nucleic acid encoding said oncogenic fusion protein.
- 20 8. The method of claim 1 wherein said identifying comprises using an antibody to identify said fusion protein.
9. The method of claim 1 wherein said identifying comprises using a cytochemical technique.
10. The method of claim 9 wherein said cytochemical technique employs nucleic acid  
25 hybridization.

11. The method of claim 10 wherein said cytochemical technique is FISH.
12. The method of claim 1 wherein said disease is a hematopoietic disorder.
13. The method of claim 11 wherein said hematopoietic disorder is selected from the group consisting of a T or B cell lymphoma, CML, APL, ALL, AML, NHL, and CMML.
- 5 14. The method of claim 1 wherein said disease is characterized by a solid tumor.
15. The method of claim 14 wherein said solid tumor is selected from the group consisting of papillary thyroid carcinoma, Ewing's sarcoma, melanoma, liposarcoma, rhabdomyosarcoma, synovial sarcoma.
- 10 16. The method of claim 1 wherein said fusion protein contains one or more functional domains or portions thereof selected from the group consisting of kinases and DNA binding motifs.
17. The method of claim 12 or 13 wherein said administering employs an *ex vivo* procedure.
- 15 18. The method of claim 14 wherein said administering is intralesional.
19. The method of claim 1 wherein said administering is parenteral.
20. The method of claim 1 wherein said HSP90-inhibiting compound has an  $IC_{50}$  at least two-fold higher for cells that do not have characteristics indicative of said genetically-defined proliferative disorder relative to those cells that do have such
- 20 characteristics.
21. The method of claim 1 wherein said HSP90-inhibiting compound has an  $IC_{50}$  at least five-fold higher for cells that do not have characteristics indicative of said genetically-defined proliferative disorder relative to those cells that do have such characteristics.

22. The method of claim 1 wherein said HSP90-inhibiting compound has an IC<sub>50</sub> at least ten-fold higher for cells that do not have characteristics indicative of said genetically-defined proliferative disorder relative to those cells that do have such characteristics.

23. The method of claim 1 wherein cells of said patient are monitored *in vitro* for sensitivity prior to administration of said compound to said patient.

24. The method of claim 1 wherein said non-random chromosomal aberration is a translocation.

25. The method of claim 1 wherein said non-random chromosomal aberration is a inversion.

26. The method of claim 1 wherein said non-random chromosomal aberration is a deletion.

27. The method of claim 1 wherein said non-random chromosomal aberration is selected from the group consisting of inv14 (q11; q32), t(9; 22)(q34; q11), t(1; 19)(q23; p13.3), t(17; 19)(q22; p13), t(15; 17)(q21-q11-22), t(11; 17)(q23; q21.1), t(4; 11)(q21; q23), t(9; 11)(q21; q23), t(11; 19)(q23; p13), t(X; 11)(q13; q23), t(1; 11)(p32; q23), t(6; 11)(q27; q23), t(11; 17)(q23; q21), t(8; 21)(q22; q22), t(3; 21)(q26; q22), 5(16; 21)(p11; q22), t(6; 9)(p23; q34), t(4; 16)(q26; p13), inv(2; 2)(p13; p11.2-14), inv(16)(p13q22), t(5; 12)(q33; p13), t(2; 5)(2p23; q35), t(9; 12)(q34; p13), del(12p), t(15; 17)(q22; q12), t(11; 17)(q23; q12), t(16; 16)(p13; q22), inv(16)(p13; q22), t(9; 11)(p22; q23), t(1; 22)(p13; q13), t(3; 3)(q21; q26), inv(3)(q21q26), t(3; 5)(q21; q31), t(3; 5)(q25; q34), t(7; 11)(p15; p15), t(8; 16)(p11; p13), t(9; 12)(q34; p13), t(12; 22)(p13; q13), del(5q), del(7q), del(20q), t(11q23), t(12; 21)(p13; q22), t(5; 12)(q31; p13), t(1; 12)(q25; p13), t(12; 15)(p13; q25), t(1; 12)(q21; p13), t(12; 21)(q13; p32), and t(5; 7)(q33; q11.2)).

28. The method of claim 1 wherein said non-random chromosomal aberration is a t(9; 22)(q34; q11) optionally characterized by and comprising a sequence selected from any one of SEQ ID NOs 15-26 or a homolog, isoform, or allelic variation thereof.

29. A method of treating cancerous cells in a heterogeneous population of cells, said heterogeneous population comprising both cancerous and noncancerous, and said

cancerous cells characterized by fusion proteins not found in said noncancerous cells, said method comprising:

administering to said heterogeneous population of cells a pharmaceutically effective amount of an HSP90-inhibiting compound.

5 30. The method of claim 29 wherein said compound has an  $IC_{50}$  that is at least five-fold lower for said cancerous cells than for said noncancerous cells within said heterogeneous population, and wherein said pharmaceutically effective amount administered is about one half or less of the  $IC_{50}$  of said noncancerous cells.

10 31. The method of claim 29 wherein said compound has an  $IC_{50}$  that is at least ten-fold lower for said cancerous cells than for said noncancerous cells within said heterogeneous population, and wherein said pharmaceutically effective amount administered is about one half or less of the  $IC_{50}$  of said noncancerous cells.

32. The method of any of claims 29-31, wherein said compound is an ansamycin.

15 33. The method of claim 32, wherein said ansamycin is selected from the group consisting of geldanamycin, 17-AAG, herbimycin A, and macbecin.

34. The method of claim 33, wherein said ansamycin is 17-AAG.

35. The method of any of claims 29-31 wherein said HSP90-inhibiting compound is a compound that binds the ATP-binding site of a HSP90.

20 36. The method of any of claims 29-31 wherein said cancerous cells are leukemic cells.

37. The method of claim 36 wherein said leukemic cells are selected from the group consisting of a T or B cell lymphoma, CML, APL, ALL, AML, NHL, and CMML.

25 38. The method of any of claims 29-31 wherein said treatment is monitored using one or more techniques selected from the group consisting of PCR, antibody staining, and nucleic acid hybridization, and wherein said techniques are selective for the presence of cancerous cells.

The method of any of claims 29-31 wherein said genetically-defined proliferative disorder is a solid tumor.

40. The method of claim 39 wherein said solid tumor is selected from the group consisting of papillary thyroid carcinoma, Ewing's sarcoma, melanoma, liposarcoma, rhabdomyosarcoma, and synovial sarcoma.
41. The method of any of claims 29-31 wherein said fusion protein contains one or more functional domains selected from the group consisting of kinases and DNA binding motifs.
42. The method of any of claims 29-31 wherein said administering employs an *ex vivo* procedure.
43. The method of any of claims 29-31 wherein said administering is intralesional.
44. The method of any of claims 29-31 wherein said administering is parenteral.
45. The method of claim 29 wherein said fusion protein arises from a chromosomal translocation.
46. The method of claim 29 wherein said fusion protein arises from a chromosomal inversion.
47. The method of claim 29 wherein said fusion protein arises from a chromosomal deletion.
48. The method of claim 29 wherein said fusion protein is generated from a non-random chromosomal aberration selected from the group consisting of inv14 (q11; q32), t(9; 22)(q34; q11), t(1; 19)(q23; p13.3), t(17; 19)(q22; p13), t(15; 17)(q21-q11-22), t(11; 17)(q23; q21.1), t(4; 11)(q21; q23), t(9; 11)(q21; q23), t(11; 19)(q23; p13), t(X; 11)(q13; q23), t(1; 11)(p32; q23), t(6; 11)(q27; q23), t(11; 17)(q23; q21), t(8; 21)(q22; q22), t(3; 21)(q26; q22), 5(16; 21)(p11; q22), t(6; 9)(p23; q34), t(4; 16)(q26; p13), inv(2; 2)(p13; p11.2-14), inv(16)(p13q22), t(5; 12)(q33; p13), t(2; 5)(2p23; q35), t(9;12)(q34;p13), del(12p), t(15;17)(q22;q12), t(11;17)(q23;q12), t(16;16)(p13;q22), inv(16)(p13;q22), t(9;11)(p22;q23), t(1;22)(p13;q13), t(3;3)(q21;q26), inv(3)(q21q26), t(3;5)(q21;q31), t(3;5)(q25;q34), t(7;11)(p15;p15), t(8;16)(p11;p13), t(9;12)(q34;p13), t(12;22)(p13;q13),

39. The method of any of claims 29-31 wherein said genetically-defined proliferative disorder is a solid tumor.

40. The method of claim 39 wherein said solid tumor is selected from the group consisting of papillary thyroid carcinoma, Ewing's sarcoma, melanoma, liposarcoma, rhabdomyosarcoma, and synovial sarcoma.

41. The method of any of claims 29-31 wherein said fusion protein contains one or more functional domains selected from the group consisting of kinases and DNA binding motifs.

42. The method of any of claims 29-31 wherein said administering employs an *ex vivo* procedure.

43. The method of any of claims 29-31 wherein said administering is intralesional.

44. The method of any of claims 29-31 wherein said administering is parenteral.

45. The method of claim 29 wherein said fusion protein arises from a chromosomal translocation.

46. The method of claim 29 wherein said fusion protein arises from a chromosomal inversion.

47. The method of claim 29 wherein said fusion protein arises from a chromosomal deletion.

48. The method of claim 29 wherein said fusion protein is generated from a non-random chromosomal aberration selected from the group consisting of inv14 (q11; q32), t(9; 22)(q34; q11), t(1; 19)(q23; p13.3), t(17; 19)(q22; p13), t(15; 17)(q21-q11-22), t(11; 17)(q23; q21.1), t(4; 11)(q21; q23), t(9; 11)(q21; q23), t(11; 19)(q23; p13), t(X; 11)(q13; q23), t(1; 11)(p32; q23), t(6; 11)(q27; q23), t(11; 17)(q23; q21), t(8; 21)(q22; q22), t(3; 21)(q26; q22), 5(16; 21)(p11; q22), t(6; 9)(p23; q34), t(4; 16)(q26; p13), inv(2; 2)(p13; p11.2-14), inv(16)(p13q22), t(5; 12)(q33; p13), t(2; 5)(2p23; q35), t(9; 12)(q34;p13), del(12p), t(15; 17)(q22; q12), t(11; 17)(q23; q12), t(16; 16)(p13; q22), inv(16)(p13; q22), t(9; 11)(p22; q23), t(1; 22)(p13; q13), t(3; 3)(q21; q26), inv(3)(q21q26), t(3; 5)(q21; q31), t(3; 5)(q25; q34), t(7; 11)(p15; p15), t(8; 16)(p11; p13), t(9; 12)(q34; p13), t(12; 22)(p13; q13),

del(5q), del(7q), del(20q), t(11q23), t(12;21)(p13;q22), t(5;12)(q31;p13), t(1;12)(q25;p13), t(12;15)(p13;q25), t(1;12)(q21;p13), t(12;21)(q13;p32), and t(5;7)(q33;q11.2)).

49. The method of claim 29 wherein said non-random chromosomal aberration is t(9;22)(q34;q11).

5 50. The method of claim 1 or 29 wherein said fusion protein has a heightened dependence on HSP90.

51. The method of claim 20 or 29 wherein said HSP90-inhibiting compound has an IC<sub>50</sub> that is lower for cancerous cells than for noncancerous cells.

52. The method of claim 5 or 35 wherein said inhibitor is a synthetic analog of geldanamycin.

10 53. A method of treating a patient having a proliferative disease associated with a mutant protein or cellular protein isoform dependent on HSP90, comprising:

providing a cell, tissue, or fluid sample of a patient suspected of having said proliferative disease;

15 identifying in said cell, tissue, or fluid sample one or more characteristics indicative of said mutant protein or cellular protein isoform; and

administering to said patient a pharmaceutically effective amount of an HSP90-inhibiting compound.

20 54. The method of claim 53 wherein said mutant protein or cellular protein isoform is selected from the group consisting of src, RET, p53, p51, p63, p73, and homologs and allelic variations thereof.

55. The method of claim 53 wherein said mutant protein or cellular protein isoform is a dominant negative mutant.

25 56. The method of claim 53 wherein said mutant protein or cellular protein isoform is a human p53 selected from the group consisting of N239S, C176R, and R213\*, Y236delta, C176Y, M133T, G245D, E258K, 1-293delta, G245C, R248W, E258K, R282W, R175H,



R280K, V143A, R175H, P177S, H178P, H179R, R181P, 238-9delta, G245S, G245D, M246R, R248Q, R249S, R273H, R273C, R273L, and D281Y.

57. The method of claim 53 wherein said mutant protein or cellular protein isoform is a dominant positive mutant.

5 58. The method of claim 57 wherein said mutant protein or cellular protein isoform is a C176Y mutant.

59. The method of claim 53 wherein said patient is heterozygous for said mutant protein or cellular protein isoform.

60. The method of claim 59 wherein said mutant protein or cellular protein isoform is p53 and wherein said proliferative disease is rheumatoid arthritis.  
10

61. The method of claim 53, wherein said compound is an ansamycin.

62. The method of claim 61, wherein said ansamycin is selected from the group consisting of geldanamycin, 17-AAG, herbimycin A, and macbecin.

63. The method of claim 62, wherein said ansamycin is 17-AAG.

15 64. The method of claim 53, wherein said inhibitor is a compound that binds into the ATP-binding site of a HSP90.

65. The method of claim 64 wherein said compound is radicicol or an analog thereof.

66. The method of claim 53 wherein said identifying comprises using at least one technique selected from the group consisting of nucleic acid hybridization, PCR, LCR, antibody staining, and immunoprecipitation to determine the presence of said mutant protein or cellular protein isoform.  
20

67. The method of claim 53 wherein said administering employs an *ex vivo* procedure.

68. The method of claim 53 wherein said administering is intralesional.

69. The method of claim 53 wherein said administering is parenteral.

70. The method of claim 53 wherein said HSP90-inhibiting compound has an  $IC_{50}$  at least two-fold higher for cells that do not have characteristics indicative of said mutant protein or cellular protein isoform relative to those cells that do have such characteristics.

71. The method of claim 53 wherein said HSP90-inhibiting compound has an  $IC_{50}$  at least ten-fold higher for cells that do not have characteristics indicative of said mutant protein or cellular protein isoform relative to those cells that do have such characteristics.

72. The method of claim 53 wherein cells of said patient are monitored *in vitro* for sensitivity prior to administration of said compound to said patient.

73. A method of selectively treating cells that express a mutant protein or cellular protein isoform that gives rise to a proliferative disorder dependent on HSP90, said method comprising:

providing a population of cells in which at least some of said population express a mutant protein or cellular protein isoform that is differentially dependent on HSP90 for effect and gives rise to a proliferative disorder, and

administering to said population a pharmaceutically effective amount of an HSP90-inhibiting compound.

74. The method of claim 73 wherein said compound has an  $IC_{50}$  that is at least five-fold lower for said cells that express said mutant protein or cellular protein isoform than for those cells that do not, and wherein said pharmaceutically effective amount administered is about one half or less of the  $IC_{50}$  of cells that do not express said mutant protein or cellular protein isoform.

75. The method of claim 73 wherein said compound has an  $IC_{50}$  that is at least ten-fold lower for said cells that express said mutant protein or cellular protein isoform than for those cells that do not, and wherein said pharmaceutically effective amount administered is about one half or less of the  $IC_{50}$  of cells that do not express said mutant protein or cellular protein isoform..

76. The method according to any of claims 73-75, wherein said compound is an ansamycin.

77. The method of claim 76, wherein said ansamycin is selected from the group consisting of geldanamycin, 17-AAG, herbimycin A, or macbecin.
78. The method of claim 77, wherein said ansamycin is 17-AAG.
79. The method of any of claims 73-75, wherein said compound is a compound that  
5 binds the ATP-binding site of a HSP90.
80. The method of claim 79 wherein said compound is radicicol or an analog thereof.
81. The method of any of claims 73-75 wherein said treatment is monitored using one or more techniques selected from the group consisting of PCR, LCR, nucleic acid hybridization, antibody labeling, and immunoprecipitation, and wherein said techniques  
10 are selective for the presence of said mutant protein or cellular protein isoform.
82. The method of any of claims 73-75 wherein said administering employs an *ex vivo* procedure.
83. The method of any of claims 73-75 wherein said administering is intralesional.
84. The method of any of claims 73-75 wherein said administering is parenteral.
- 15 85. The method of claim 76 wherein said HSP90-inhibiting compound has an  $IC_{50}$  that is lower for cells expressing the mutant protein or cellular protein isoform than for cells that do not express said mutant protein or cellular protein isoform.
86. The method of claim 64 or 73 wherein said inhibitor is a synthetic analogue of geldanamycin.
- 20 87. The method of claim 73 wherein said mutant protein or cellular protein isoform is selected from the group consisting of src, RET, p53, p51, p63, p73, and homologs and allelic variations thereof.
88. The method of claim 73 wherein said mutant protein or cellular protein isoform is a dominant negative mutant.

89. The method of claim 88 wherein said mutant protein or cellular protein isoform is a human p53 selected from the group consisting of N239S, C176R, and R213\*, Y236delta, C174Y, M133T, G245D, E258K, 1-293delta, G245C, R248W, E258K, R282W, R175H, R280K, V143A, R175H, P177S, H178P, H179R, R181P, 238-9delta, G245S, G245D,  
5 M246R, R248Q, R249S, R273H, R273C, R273L, and D281Y.
90. The method of claim 73 wherein said mutant protein or cellular protein isoform is a dominant positive mutant.
91. The method of claim 90 wherein said mutant protein or cellular protein isoform is C176Y human p53, or a homolog thereof.
- 10 92. The method of claim 73 wherein said cells that express a mutant protein or cellular protein isoform are heterozygous for said mutant protein or cellular protein isoform.
93. The method of claim 92 wherein said mutant protein or cellular protein isoform is p53 and wherein said proliferative disease is rheumatoid arthritis or a cancer.

## FIGURE 1

<u>Type of Aberration</u>	<u>Background Literature</u>	<u>Affected Gene(s)</u>	<u>Protein Domain</u>	<u>Fusion Protein</u>	<u>Disease</u>
t(9; 22)(q34; q11)	de Klein, A. et al. Nature 300, 765-767 (1982)	<i>CABL</i> (9q34) <i>BCR</i> (22q11)	tyrosine kinase serine kinase	serine + tyrosine kinase	CML/ALL
inv14 (q11; q32)	Baer, R., Chen, K.-C., Smith, S. D. & Rabbitts, T. H. Cell 43, 705-713 (1985); Denny, C. T. et al. Nature 320, 549-551 (1986)	TCR- $\alpha$ (14q11) VH-(14q32)	TCR-C $\alpha$ Ig VH	VH-TCR-C $\alpha$	T/B-cell lymphoma
t(1; 19)(q23; p13.3)	Kamps, M. P., Murre, C., Sun, X.-H. & Baltimore, D. Cell 60, 547-555 (1990); Nourse, J. et al. Cell 60, 535-545 (1990)	<i>PBX1</i> (1q23) <i>E2A</i> (19p13.3)	HD AD-b-HLH	AD + HD	pre-B-ALL
t(17; 19)(q22; p13)	Hunger, S. P., Ohyashiki, K., Toyama, K. & Clearly, M. L. Genes Dev. 6, 1608-1620 (1992); Inaba, T. et al. Science 257, 531-534 (1992)	<i>HLF</i> (17q22) <i>E2A</i> (19p13)	bZIP AD-b-HLH	AD + bZIP	pro-B-ALL
t(15; 17)(q21-q11-22)	Giliard, E. F. & Solomon, E. Sem. Cancer Biol. 4, 359-368 (1993)	<i>PML</i> (15Q21) <i>RARA</i> (17q21)	Zinc-finger Retinoic acid receptor- $\alpha$	Zinc-finger + RAR DNA and ligand binding	APL
t(11; 17)(q23; q21.1)	Chen, Z. et al. EMBO J. 12, 1161-1167 (1993)	<i>PLZF</i> (11q23) <i>RARA</i> (17q21)	Zinc-finger Retinoic acid receptor $\alpha$	Zn-finger + RAR DNA and ligand binding	APL
t(4; 11)(q21; q23)	Djabali, M. et al. Nature Genet. 2, 113-118 (1992); Gu, Y. et al. Cell 71, 701-708 (1992)	<i>MLL</i> (11q23) <i>AF4</i> (4q21)	A-T hook/Zn-finger Ser-Pro rich	A-T hook + (Ser-pro)	ALL/preB- ALL/ ANLL
t(9; 11)(q21; q23)	Nakamura, T. et al. Proc. natn. Acad. Sci. U.S.A. 90, 4631-4635 (1993); Lida, S. et al. Oncogene 8, 3085-3092 (1993)	<i>MLL</i> (11q23) <i>AF9/MLLT3</i> (9p22)	A-T hook/Zn-finger Ser-Pro rich	A-T hook + (Ser-Pro)	ALL/preB- ALL/ ANLL
t(11; 19)(q23; p13)	Tkachuk, D. C., Kohler, S. & Cleary, M. L. Cell 71, 691-700 (1992); Yamamoto, K. et al. Oncogene 8, 2617-2625 (1993)	<i>MLL</i> (11q23) <i>ENL</i> (19p13)	A-T hook/Zn-finger Ser-Pro rich	A-T hook + Ser-Pro	pre-B-ALL/ T-ALL/ ANLL

FIGURE 1 (Cont'd)

<u>Type of Aberration</u>	<u>Background Literature</u>	<u>Affected Gene(s)</u>	<u>Protein Domain</u>	<u>Fusion Protein</u>	<u>Disease</u>
t(X; 11)(q13; q23)	Corral, J. et al. Proc. natn. Acad. Sci. U.S.A. 90, 8538-8542 (1993)	<i>MLL</i> (11q23) <i>AFXI</i> (Zq13)	A-T hook/Zn-finger Ser-Pro rich	A-T hook + (Ser-Pro)	T-ALL
t(1; 11)(p32; q23)	Bernard, O. A., Mauchauffe, M., Mecucci, C., Van Den Berghe, H. & Berger, R. Oncogene 9, 1039-1045 (1994)	<i>MLL</i> (11q23) <i>AFIP</i> (1p32)	A-T hook/Zn-finger Eps-15 homologue	A-T hook +	ALL
t(6; 11)(q27; q23)	Prasac, R. et al. Cancer Res. 53, 5624-5628 (1993)	<i>MLL</i> (11q23) <i>AF6</i> (6q27)	A-T hook/Zn-finger myosin homologue	A-T hook +	ALL
t(11; 17)(q23; q21)	Prasac, R. et al. Proc. natn. Acad. Sci. U.S.A. 91, 8107-8111 (1994)	<i>MLL</i> (11q23) <i>AF17</i> (17q21)	A-T hook/Zn-finger Cys-rich/leucine zipper	A-T hook + leucine zipper	AML
t(8; 21)(q22; q22)	Ohki, M. Sem. Cancer Biol. 4, 369-376 (1993)	<i>AML1/CBF<math>\alpha</math></i> (21q22) <i>ETO/MTG8</i> (8q22)	DNA binding/runt homology Zn-finger	DNA binding + Zn-fingers	AML
t(3; 21)(q26; q22)	Mitani, K. et al. EMBO J. 13, 504-510 (1994)	<i>AML1</i> (21q22) <i>EVI-1</i> (3q26)	DNA binding Zn-finger	DNA binding + Zn-fingers	CML
t(3; 21)(q26; q22)	Nucifora, G., Begy, C. R., Erickson, P., Drackin, H. A. & Rowley, J. D. Proc. natn. Acad. Sci. U.S.A. 90, 7784-7788 (1993)	<i>AML1</i> (21q22) <i>EAP</i> (3q26)	DNA binding Sn protein	DNA binding + out-of-frame EAP	Myelo-dysplasia
5(16; 21)(p11; q22)	Shimizu, K. et al. Proc. natn. Acad. Sci. U.S.A. 90, 10280-10284 (1993)	<i>FUS</i> (16p11) <i>ERG</i> (21q22)	Gin-Ser Tyr/Gly-rich/RNA binding Ets-like DNA binding	Gin-Ser-Tyr + DNA binding	Myeloid
t(6; 9)(p23; q34)	von Lindern, M. et al. Molec. Cell Biol. 12, 1687-1697 (1992)	<i>DEK</i> (6p23) <i>CAN</i> (9q34)	unknown ZIP	ZIP+	AML
9; 9?	von Lindern, M., Breems, D., van Baai, S., Acriansen, H. & Grosveld, G. Genes Chrom. Cancer 5, 227-234 (1992)	<i>SET</i> (9q34) <i>CAN</i> (9p34)	ZIP	ZIP+	AUL
t(4; 16)(q26; p13)	Laabi, Y. et al. EMBO J. 11, 3897-3904 (1992)	<i>IL-2</i> (4q26) <i>BCM</i> (16p13.1)	IL2 TM domain	IL-2/TM	T-lymphoma

FIGURE 1 (Cont'd)

<u>Type of Aberration</u>	<u>Background Literature</u>	<u>Affected Gene(s)</u>	<u>Protein Domain</u>	<u>Fusion Protein</u>	<u>Disease</u>
inv(2; 2)(p13; p11.2-14)	Lu, D. et al. Oncogene 6, 1235-1241 (1991)	REL (2p13) NRG (2p11.2-14)	DNA binding-activator not known	DNA binding +	NHL
inv(16)(p13q22)	Liu, P. et al. Science 261, 1041-1044 (1993)	Myosin MYH11 (16p13) CBF- $\beta$ (16q22)		DNA binding?	AML
t(5; 12)(q33; p13)	Golub, T. R., Barker, G. F., Lovett, M. & Gilliland, D. G. Cell 77, 307-316 (1994)	PDGF- $\beta$ (5q33) TEL (12p13)	Receptor kinase Ets-like DNA binding	Kinase + DNA binding	CMML
t(2; 5)(2p23; q35)	Morris, S. W. et al. Science 263, 1281-1284 (1994)	NPM (5q35) ALK (2p23)	Nuclear phosphoprotein Tyrosine kinase	N terminus NPM + kinase	NHL
t(11; 22)(q24; q12)	Delattre, O. et al. Nature 359, 162-165 (1992)	FLII (11q24) EWS (22q12)	Ets-like DNA binding Gin-Ser-Tyr/Gly- rich/RNA binding	Gin-Ser-Tyr + DNA binding	Ewing's sarcoma
inv10(q11.2; q21)	Pierotti, M. A. et al. Proc. natn. Acad. Sci. U.S.A. 89, 1616-1620 (1992)	RET (10q11.2) D10S170 (q21)	tyrosine kinase uncharacterized	Unk + tyrosine kinase	Papillary thyroid carcinoma
t(12; 22)(q13; q12)	Zucman, J. et al. Nature Genet. 4, 341-345 (1993)	ATF1 (12q13) EWS (22q12)	bZIP Gln-Ser-Tyr/Gly- rich/RNA binding	Gin-Ser-Tyr + bZIP	a melanoma
t(12; 16)(q13; p11)	Crozat, A., Aman, P., Mandahl, N. & Ron, D. Nature 363, 640-644 (1993); Rabbitts, T. H. ; Forster, A., Larson, R. & Nathan, P. Nature Genet. 4, 175-180 (1993)	CHOP (12q13) FUS (16p11)	(DNA binding?)/ZIP Gln-Ser-Tyr/Gly- rich/RNA binding	Gin-Ser-Tyr +(DNA binding?)/ZIP	Liposarcoma
t(2; 13)(q35; q14)	Ben-David, Y., Giddens, E. B., Letwin, K. & Bernstein, A. Genes Dev. 5, 908-918 (1991)	PAX3 (2q35) FKHR (13q14)	Paired box/homeodomain Forkhead domain	PB/HD +DNA binding	Rhabdomyosarcoma
t(X; 18)(p11.2;q11.2)	Clark, J. et al. Nature Genet. 7, 502-5087 (1994)	SYT (18q11.2) SSX (Xp11.2)	None identified None identified		Synovial sarcoma

1/299

## SEQUENCE LISTING

&lt;110&gt; CONFORMA THERAPEUTICS CORP.

<120> METHODS FOR TREATING GENETICALLY-DEFINED PROLIFERATIVE  
DISORDERS WITH HSP90 INHIBITORS

&lt;130&gt; 031164.0010WO

&lt;140&gt;

&lt;141&gt;

&lt;150&gt; 60/272,751

&lt;151&gt; 2001-03-01

&lt;160&gt; 330

&lt;170&gt; PatentIn Ver. 2.1

&lt;210&gt; 1

&lt;211&gt; 46

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

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Ser	Ser	Glu	Lys	Leu	Arg	Val	Leu	Gly	Tyr	Asn	His	Asn	Gly
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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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ggctataatc	acaatgggga					140

&lt;210&gt; 3

&lt;211&gt; 561

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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tttaagcaga	gttcaagaag	aagccatacg	gtgaaccagg	tgatgctgag	gttatctgga	240
tccaggccat	gcagatgaag	ccatatttac	ctttgtgata	ttggggctga	tcttggagct	300
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2/299

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gagacatttg ggctggaatt c 561

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&lt;210&gt; 4

&lt;211&gt; 284

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 4

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Thr Gln Gln Tyr Asp Cys Lys Trp Tyr Ile Pro Val Thr Asp Leu Ser
      20          25          30

Phe Gln Met Val Asp Glu Leu Glu Ala Val Pro Asn Ile Pro Leu Val
      35          40          45

Pro Asp Glu Glu Leu Asn Ala Leu Lys Ile Lys Ile Ser Gln Ile Lys
      50          55          60

Ser Asp Ile Gln Arg Glu Lys Arg Ala Asn Lys Gly Ser Lys Ala Thr
      65          70          75          80

Glu Arg Leu Lys Lys Lys Leu Ser Glu Gln Glu Ser Leu Leu Leu Leu
      85          90          95

Met Ser Pro Ser Met Ala Phe Arg Val His Ser Arg Asn Gly Lys Ser
      100          105          110

Tyr Thr Phe Leu Ile Ser Ser Asp Tyr Glu Arg Ala Glu Trp Arg Glu
      115          120          125

Asn Ile Arg Glu Gln Gln Lys Lys Cys Phe Arg Ser Phe Ser Leu Ala
      130          135          140

Ser Val Glu Leu Gln Met Leu Thr Asn Ser Cys Val Lys Leu Gln Thr
      145          150          155          160

Val His Ser Ile Pro Leu Thr Ile Asn Lys Glu Asp Asp Glu Ser Pro
      165          170          175

Gly Leu Tyr Gly Phe Leu Asn Val Ile Val His Ser Ala Thr Gly Phe
      180          185          190

Lys Gln Ser Ser Lys Leu Gln Arg Pro Val Ala Ser Asp Phe Glu Pro
      195          200          205

Gln Gly Leu Ser Glu Ala Ala Arg Trp Asn Ser Lys Glu Asn Leu Leu
      210          215          220

Ala Gly Pro Ser Glu Asn Asp Pro Asn Leu Phe Val Ala Leu Tyr Asp
      225          230          235          240

Phe Val Ala Ser Gly Asp Asn Thr Leu Ser Ile Thr Lys Gly Glu Lys

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3/299

	245		250		255
Leu Arg Val	Leu Gly Tyr Asn His	Asn Gly Glu Trp Cys	Glu Ala Gln		
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	275	280			

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 ccagtagcat ctgactttga gcctcagggt ctgagtgaag ccgctcgttg gaactccaag 660  
 gaaaaccttc tcgctggacc cagtgaataa gacccaacc ttttcgttgc actgtatgat 720  
 tttgtggcca gtggagataa cactctaagc ataactaaag gtgaaaagct cggggtctta 780  
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 cggccagtag catctgactt tgagcctcag ggtctgagtg aagccgctcg ttggaactcc 180  
 aaggaaaacc ttctcgtcgg acccagtga aatgaccca accttttcgt tgcaactgat 240  
 gatcttctgg ccagtggaga taacactcta agcataacta aaggtgaaaa gctccgggtc 300  
 ttaggctata atcacaatgg ggaatggtgt gaagcccaaa ccaaaaatgg ccaaggctgg 360  
 gtccaagca actacatcac gccagtcaac agtctggaga aacactcctg gtaccatggg 420  
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Gly Ser Lys Ala Thr Glu Arg Leu Lys Lys Lys Leu Ser Glu Gln Glu

4/299

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 Ser Leu Leu Leu Leu Met Ser Pro Ser Met Ala Phe Arg Val His Ser  
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 Arg Asn Gly Lys Ser Tyr Thr Phe Leu Ile Ser Ser Asp Tyr Glu Arg  
 50 55 60  
 Ala Glu Trp Arg Glu Asn Ile Arg Glu Gln Gln Lys Lys Cys Phe Arg  
 65 70 75 80  
 Ser Phe Ser Leu Ala Ser Val Glu Leu Gln Met Leu Thr Asn Ser Cys  
 85 90 95  
 Val Lys Leu Gln Thr Val His Ser Ile Pro Leu Thr Ile Asn Lys Glu  
 100 105 110  
 Asp Asp Glu Ser Pro Gly Leu Tyr Gly Phe Leu Asn Val Ile Val His  
 115 120 125  
 Ser Ala Thr Gly Phe Lys Gln Ser Ser Lys Leu Gln Arg Pro Val Ala  
 130 135 140  
 Ser Asp Phe Glu Pro Gln Gly Leu Ser Glu Ala Ala Arg Trp Asn Ser  
 145 150 155 160  
 Lys Glu Asn Leu Leu Ala Ala Pro Ser Glu Asn Asp Pro Asn Leu Phe  
 165 170 175  
 Val Ala Leu Tyr Asp Phe Val Ala Ser Gly Asp Asn Thr Leu Ser Ile  
 180 185 190  
 Thr Lys Gly Glu Lys Leu Arg Val Leu Gly Tyr Asn His Asn Gly Glu  
 195 200 205  
 Trp Cys Glu Ala Gln Thr Lys Ile Gly Gln Gly Trp Val Pro Ser Asn  
 210 215 220  
 Tyr  
 225

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&lt;211&gt; 679

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 8

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 ccagcatggc cttcaggggtg cacagccgca acggcaagag ttacacgttc ctgatctcct 180  
 ctgactatga gcgtgcagag tggagggaga acatccggga gcagcagaag aagtgtttca 240  
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5/299

tcttaggcta taatcacaat ggggaatggt gtgaagccca aacccaaaatt ggccaaggct 660  
 gggttccaag caactacat 679

&lt;210&gt; 9

&lt;211&gt; 332

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 9

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Glu Gln Glu Ser Leu Leu Leu Leu Met Ser Pro Ser Met Ala Phe Arg  
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Val His Ser Arg Asn Gly Lys Ser Tyr Thr Phe Leu Ile Ser Ser Asp  
 35 40 45

Tyr Glu Arg Ala Glu Trp Arg Glu Asn Ile Arg Glu Gln Gln Lys Lys  
 50 55 60

Cys Phe Arg Ser Phe Ser Leu Thr Ser Val Glu Leu Gln Met Leu Thr  
 65 70 75 80

Asn Ser Cys Val Lys Leu Gln Thr Val His Ser Ile Pro Leu Thr Ile  
 85 90 95

Asn Lys Glu Asp Asp Glu Ser Pro Gly Leu Tyr Gly Phe Leu Asn Val  
 100 105 110

Ile Val His Ser Ala Thr Gly Phe Lys Gln Ser Ser Lys Ala Leu Gln  
 115 120 125

Arg Pro Val Ala Ser Asp Phe Glu Pro Gln Gly Leu Ser Glu Ala Ala  
 130 135 140

Arg Trp Asn Ser Lys Glu Asn Leu Leu Ala Gly Pro Ser Glu Asn Asp  
 145 150 155 160

Pro Asn Leu Phe Val Ala Leu Tyr Asp Phe Val Ala Ser Gly Asp Asn  
 165 170 175

Thr Leu Ser Ile Thr Lys Gly Glu Lys Leu Arg Val Leu Gly Tyr Asn  
 180 185 190

His Asn Gly Glu Trp Cys Glu Ala Gln Thr Lys Asn Gly Gln Gly Trp  
 195 200 205

Val Pro Ser Asn Tyr Ile Thr Pro Val Asn Ser Leu Glu Lys His Ser  
 210 215 220

Trp Tyr His Gly Pro Val Ser Arg Asn Ala Ala Glu Tyr Leu Leu Ser  
 225 230 235 240

Ser Gly Ile Asn Gly Ser Phe Leu Val Arg Glu Ser Glu Ser Ser Pro  
 245 250 255

6/299

Gly Gln Arg Ser Ile Ser Leu Arg Tyr Glu Gly Arg Val Tyr His Tyr  
 260 265 270

Arg Ile Asn Thr Ala Ser Asp Gly Lys Leu Tyr Val Ser Ser Glu Ser  
 275 280 285

Arg Phe Asn Thr Leu Ala Glu Leu Val His His His Ser Thr Val Ala  
 290 295 300

Asp Gly Leu Ile Thr Thr Leu His Tyr Pro Ala Pro Lys Arg Asn Lys  
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Pro Thr Val Tyr Gly Val Ser Pro Asn Tyr Asp Lys  
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&lt;213&gt; Homo sapiens

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&lt;210&gt; 11

&lt;211&gt; 101

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 11

Arg Glu Gln Gln Lys Lys Cys Phe Arg Ser Phe Ser Leu Thr Ser Val  
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Glu Leu Gln Met Leu Thr Asn Ser Cys Val Lys Leu Gln Thr Val His  
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Ser Ile Pro Leu Thr Ile Asn Lys Glu His Asp Glu Ser Pro Gly Leu  
 35 40 45

Tyr Gly Phe Leu Asn Val Ile Val His Ser Ala Thr Gly Phe Lys Gln  
 50 55 60

7/299

Ser Ser Asn Leu Tyr Cys Thr Leu Glu Val Asp Ser Phe Gly Tyr Phe  
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Val Asn Lys Ala Lys Thr Arg Val Tyr Arg Asp Thr Ala Glu Pro Asn  
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Leu Leu Ala Gly Pro  
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Pro Pro Gly Tyr Gly

8/299

20

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ttt 63

<210> 19  
<211> 140  
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His Asp Leu Leu Lys His Thr Pro Ala Ser His Pro Asp His Pro Leu  
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35 40 45  
Glu Glu Ile Thr Pro Arg Arg Gln Ser Met Thr Val Lys Lys Gly Glu  
50 55 60  
Gly Glu Asp Arg Met Lys Ala Ser Ser Thr Arg Lys Arg Leu Leu Leu  
65 70 75 80  
Met Glu Glu Ala Leu Gln Arg Pro Val Ala Ser Asp Phe Glu Pro Gln

9/299

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Gly Leu Ser Glu Ala Ala Arg Trp Asn Ser Lys Glu Asn Leu Leu Ala					
	100		105		110
Gly Pro Ser Glu Asn Asp Pro Asn Leu Phe Val Ala Leu Tyr Asp Phe					
	115		120		125
Val Ala Ser Gly Asp Asn Thr Leu Ser Ile Thr Lys					
	130		135		140

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 Val His Ser Arg Asn Gly Lys Ser Tyr Thr Phe Leu Ile Ser Ser Asp  
 35 40 45  
 Tyr Glu Arg Ala Glu Trp Arg Glu Asn Ile Arg Glu Gln Gln Lys Lys  
 50 55 60  
 Cys Phe Arg Ser Phe Ser Leu Thr Ser Val Glu Leu Gln Met Leu Thr  
 65 70 75 80  
 Asn Ser Cys Val Lys Leu Gln Thr Val His Ser Ile Pro Leu Thr Ile  
 85 90 95  
 Asn Lys Glu Glu Ala Leu Gln Arg Pro Val Ala Ser Asp Phe Glu Pro  
 100 105 110  
 Gln Gly Leu Ser Glu Ala Ala Arg Trp Asn Ser Lys Glu Asn Leu Leu  
 115 120 125



10/299

Ala Gly Pro Ser Glu Asn Asp Pro Asn Leu Phe Val Ala Leu Tyr Asp  
 130 135 140

Phe Val Ala Ser Gly Asp Asn Thr Leu Ser Ile Thr Lys Gly Glu Lys  
 145 150 155 160

Leu Arg Val Leu Gly Tyr Asn His Asn Gly Glu Trp Cys Glu Ala Gln  
 165 170 175

Thr Lys Asn Gly Gln Gly Trp Val Pro Ser Asn Tyr Ile Thr Pro Val  
 180 185 190

Asn Ser Leu Glu Lys His Ser Trp Tyr His Gly Pro Val Ser Arg Asn  
 195 200 205

Ala Ala Glu Tyr Leu Leu Ser Ser Gly Ile Asn Gly Ser Phe Leu Val  
 210 215 220

Arg Glu Ser Glu Ser Ser Pro Gly Gln Arg Ser Ile Ser Leu Arg Tyr  
 225 230 235 240

Glu Gly Arg Val Tyr His Tyr Arg Ile Asn Thr Ala Ser Asp Gly Lys  
 245 250 255

Leu Tyr Val Ser Ser Glu Ser Arg Phe Asn Thr Leu Ala Glu Leu Val  
 260 265 270

His His His Ser Thr Val Ala Asp Gly Leu Ile Thr Thr Leu His Tyr  
 275 280 285

Pro Ala Pro Lys Arg Asn Lys Pro Thr Val Tyr Gly Val Ser Pro Asn  
 290 295 300

Tyr Asp Lys  
 305

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&lt;211&gt; 922

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 22

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 aactcgtgtg tgaaactcca gactgtccac agcattccgc tgaccatcaa taaggaagaa 300  
 gcccttcagc ggccagtagc atctgacttt gagcctcagg gtctgagtga agccgctcgt 360  
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11/299

gtgtccccca actacgacaa gt

922

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&lt;211&gt; 359

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 23

Tyr Gln Pro Tyr Gln Ser Ile Tyr Val Gly Gly Met Met Glu Gly Glu  
 1 5 10 15

Gly Lys Gly Pro Leu Leu Arg Ser Gln Ser Thr Ser Glu Gln Glu Lys  
 20 25 30

Arg Leu Thr Trp Pro Arg Arg Ser Tyr Ser Pro Arg Ser Phe Glu Asp  
 35 40 45

Cys Gly Gly Gly Tyr Thr Pro Asp Cys Ser Ser Asn Glu Asn Leu Thr  
 50 55 60

Ser Ser Glu Glu Asp Phe Ser Ser Gly Gln Ser Ser Arg Val Ser Pro  
 65 70 75 80

Ser Pro Thr Thr Tyr Arg Met Phe Arg Asp Lys Ser Arg Ser Pro Ser  
 85 90 95

Gln Asn Ser Gln Gln Ser Phe Asp Ser Ser Ser Pro Pro Thr Pro Gln  
 100 105 110

Cys His Lys Arg His Arg His Cys Pro Val Val Val Ser Glu Ala Thr  
 115 120 125

Ile Val Gly Val Arg Lys Thr Gly Gln Ile Trp Pro Asn Asp Gly Glu  
 130 135 140

Gly Ala Phe His Gly Asp Ala Glu Ala Leu Gln Arg Pro Val Ala Ser  
 145 150 155 160

Asp Phe Glu Pro Gln Gly Leu Ser Glu Ala Ala Arg Trp Asn Ser Lys  
 165 170 175

Glu Asn Leu Leu Ala Gly Pro Ser Glu Asn Asp Pro Asn Leu Phe Val  
 180 185 190

Ala Leu Tyr Asp Phe Val Ala Ser Gly Asp Asn Thr Leu Ser Ile Thr  
 195 200 205

Lys Gly Glu Lys Leu Arg Val Leu Gly Tyr Asn His Asn Gly Glu Trp  
 210 215 220

Cys Glu Ala Gln Thr Lys Asn Gly Gln Gly Trp Val Pro Ser Asn Tyr  
 225 230 235 240

Ile Thr Pro Val Asn Ser Leu Glu Lys His Ser Trp Tyr His Gly Pro  
 245 250 255

Val Ser Arg Asn Ala Ala Glu Tyr Leu Leu Ser Ser Gly Ile Asn Gly

270

Val Ser Pro Asn Tyr Asp Lys  
355

Ala Phe His Gly Asp Ala Gly Lys Ser Pro Gly Leu Arg Leu Asn His  
20 25 30

13/299

Asn Gly

<210> 26  
 <211> 106  
 <212> DNA  
 <213> Homo sapiens

<400> 26  
 tcgtgggcgt ccgcaagacc gggcagatct ggcccaacga tggcgagggc gccttccatg 60  
 gagacgcagg taaaagcccc ggtccttaggc taaatcacia tgggga 106

<210> 27  
 <211> 114  
 <212> PRT  
 <213> Homo sapiens

<400> 27  
 Met Ala Glu Cys Pro Thr Leu Gly Glu Ala Val Thr Asp His Pro Asp  
     1                    5                    10                    15  
 Arg Leu Trp Ala Trp Glu Lys Phe Val Tyr Leu Asp Glu Lys Gln His  
                     20                    25                    30  
 Ala Trp Leu Pro Leu Thr Ile Glu Ile Lys Asp Arg Leu Gln Leu Arg  
             35                    40                    45  
 Val Leu Leu Arg Arg Glu Asp Val Val Leu Gly Arg Pro Met Thr Pro  
     50                    55                    60  
 Thr Gln Ile Gly Pro Ser Leu Leu Pro Ile Met Trp Gln Leu Tyr Pro  
     65                    70                    75                    80  
 Asp Gly Arg Tyr Arg Ser Ser Asp Ser Ser Phe Trp Arg Leu Val Tyr  
                     85                    90                    95  
 His Ile Lys Ile Asp Gly Val Glu Asp Met Leu Leu Glu Leu Leu Pro  
             100                    105                    110

Asp Asp

<210> 28  
 <211> 1324  
 <212> DNA  
 <213> Homo sapiens

<400> 28  
 cttgagaggg tctggtcttt gcttcttagg cgccccgagg acgccatggc cgagtgcccg 60  
 aactcgggg aggcagtcac cgaccaccg gaccgcctgt gggcctggga gaagttcgtg 120  
 tatttggacg agaagcagca cgcctggctg cccttaacca tcgagataaa ggatagggtta 180  
 cagttacggg tgctcttgcg tcgggaagac gtcgtcctgg ggaggcctat gacccccacc 240  
 cagataggcc caagcctgct gcctatcatg tggcagctct accctgatgg acgataccga 300  
 tcctcagact ccagtttctg gcgcttagtg taccacatca agattgacgg cgtggaggac 360  
 atgcttctcg agctgctgcc agatgactga tgtatggtct tggcagcacc tgtctccttt 420

14/299

```

caccccaggg cctgagcctg gccagcctac aatgggggatg ttgtgtttct gttcaccttc 480
gtttactatg cctgtgtctt ctccaccacg ctgggggtctg ggaggaatgg acagacagag 540
gatgagctct acccagggcc tgcaggacct gcctgtagcc cactctgctc gccttagcac 600
taccactcct gccaaaggagg attccatttg gcagagcttc ttccagggtgc ccagctatac 660
ctgtgcctcg gcttttctca gctggatgat ggtcttcagc ctctttctgt cccttctgtc 720
cctcacagca ctagtatctt atgttgcaca cccactcagc tccgtgaact tgtgagaaca 780
cagccgattc acctgagcag gacctctgaa accctggacc agtgggtctca catgggtgcta 840
cgctgcatg taaacacgcc tgcaaacgct gcctgccggg aaacacgcct gcaaacgctg 900
cctgcccgtg aacacgcctg caaacgctgc ctgcccacac aggttcacgt gcagctcaag 960
gaaaggcctg aaaggagccc ttatctgtgc tcaggactca gaagcctctg ggtcagtggg 1020
ccacatcccg ggacgcagca ggaggccagg ccggcgagcc ctgtggatga gccctcagaa 1080
cccttggtt gccacgtgg aaaagggata gaggttgggt ttccccctt tatagatggg 1140
cacgcacctg ggtgttaca agttgtatgt ggcataaata ctttttgtaa tgattgatta 1200
aatgcaagat agtttatcta acttcgtgcg caatcagctt ctatcettga cttagattct 1260
ggtggagaga agtgagaata ggcagcccc aaataaaaaa tattcatgga aaaaaaaaaa 1320
aaaa                                           1324

```

&lt;210&gt; 29

&lt;211&gt; 114

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 29

```

Met Ala Glu Cys Pro Thr Leu Gly Glu Ala Val Thr Asp His Pro Asp
  1             5             10             15

```

```

Arg Leu Trp Ala Trp Glu Lys Phe Val Tyr Leu Asp Glu Lys Gln His
      20             25             30

```

```

Ala Trp Leu Pro Leu Thr Ile Glu Ile Lys Asp Arg Leu Gln Leu Arg
      35             40             45

```

```

Val Leu Leu Arg Arg Glu Asp Val Val Leu Gly Arg Pro Met Thr Pro
      50             55             60

```

```

Thr Gln Ile Gly Pro Ser Leu Leu Pro Ile Met Trp Gln Leu Tyr Pro
      65             70             75             80

```

```

Asp Gly Arg Tyr Arg Ser Ser Asp Ser Ser Phe Trp Arg Leu Val Tyr
      85             90             95

```

```

His Ile Lys Ile Asp Gly Val Glu Asp Met Leu Leu Glu Leu Leu Pro
      100            105            110

```

Asp Asp

&lt;210&gt; 30

&lt;211&gt; 1324

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 30

```

cttgagaggc tctggctctt gcttcttagg cggccccgagg acgccatggc cgagtgcccg 60
acactcgggg aggcatcac cgaccaccgg gaccgcctgt gggcctggga gaagttcgtg 120
tatttggaag agaagcagca cgcttggtg cccttaacca tcgagataaa ggatagggtta 180
cagttacggg tgctcttgcg tcgggaagac gtcgtcctgg ggaggcctat gacccccacc 240

```

15/299

```

cagataggcc caagcctgct gcctatcatg tggcagctct accctgatgg acgataccga 300
tcctcagact ccagtttctg gcgcttagtg taccacatca agattgacgg cgtggaggac 360
atgcttctcg agctgctgcc agatgactga tgtatggtct tggcagcacc tgtctccttt 420
cacccagggg cctgagcctg gccagcctac aatggggatg ttgtgtttct gttcaccttc 480
gtttactatg cctgtgtctt ctccaccacg ctgggggtctg ggaggaatgg acagacagag 540
gatgagctct acccagggcc tgcaggacct gcctgtagcc cactctgctc gccttagcac 600
taccactcct gccaaaggagg attccatttg gcagagcttc ttccagggtgc ccagctatac 660
ctgtgcctcg gcttttctca gctggatgat ggtcttcagc ctctttctgt cccttctgtc 720
cctcacagca ctagtatttc atgttgacac cccactcagc tccgtgaact tgtgagaaca 780
cagccgattc acctgagcag gacctctgaa accctggacc agtgggtctca catgggtgcta 840
cgctgcatg taaacacgcc tgcaaacgct gcctgccggt aaacacgcct gcaaacgctg 900
cctgcccgtg aacacgcctg caaacgctgc ctgcccacac aggttcacgt gcagctcaag 960
gaaaggcctg aaaggagccc ttatctgtgc tcaggactca gaagcctctg ggtcagtggg 1020
ccacatcccg ggacgcagca ggaggccagg ccggcgagcc ctgtggatga gccctcagaa 1080
cccttggtctt gccacgtgg aaaagggata gaggttgggt ttccccctt tatagatggg 1140
cacgcacctg ggtgttataa agttgtatgt ggcataaata ctttttgtaa tgattgatta 1200
aatgcaagat agtttatcta acttcgtgcg caatcagctt ctatccttga cttagattct 1260
ggtggagaga agtgagaata ggcagccccc aaataaaaaa tattcatgga aaaaaaaaaa 1320
aaaa                                             1324

```

<210> 31  
 <211> 560  
 <212> DNA  
 <213> Homo sapiens

```

<400> 31
gtcgactgtg agttcccagc agaggcccag agtcccggtc cggcagccga ggggaagcggg 60
ggggtcttcc agaagaagaa agggccaagg tcaccccggg gcctctccag cagcagcaga 120
gggcggcggg cgggtgtcgt gctggccggg gcctcgagga aggcgcgggc cagctggggc 180
cgggtctgcy ttcccaggag ctgccaccgt tccaggggagc aagtcaggcc gggacgttag 240
cgctgcgcy ggacctcac ttgccaccaaa ggaccccaca aaccccgccc catccttagc 300
gcctgcgcy gacctcact tgccaccaag acccccacaa accccgcccc atcctgcctt 360
acgccccgcc ccaaggctgt tctcccgacc cggggtcccc cccaagacc gtcctccgcg 420
ccgcgcgtt ggtggcggcc gcatgctgcc cggatataaa gggtcggccc cacatcccag 480
ggaccagcga gcggccttga gaggtctctg ctcttgcttc ttaggcggcc cgaggacgcc 540
atggccgagt gcccgacact                                     560

```

<210> 32  
 <211> 125  
 <212> PRT  
 <213> Homo sapiens

```

<400> 32
Phe Ala Gly Val Gln Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly
  1              5              10             15

Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
      20              25              30

Phe Thr Phe Ser Ser Tyr Trp Met His Trp Val Arg Gln Ala Pro Gly
  35              40              45

Lys Gly Leu Val Trp Val Ser Arg Ile Asn Ser Asp Gly Ser Ser Thr
  50              55              60

Ser Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn

```

16/299

65		70		75		80
Ala Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp						
	85		90		95	
Thr Ala Val Tyr Tyr Cys Ala Arg Asp Pro Thr Gly Gly Ser Tyr Ile						
	100		105		110	
Pro Thr Phe Gly Arg Gly Thr Ser Leu Ile Val His Pro						
	115		120		125	

<210> 33  
 <211> 375  
 <212> DNA  
 <213> Homo sapiens

<400> 33  
 tttgcaggtg tccagtgatga ggtgcagctg gtggagtccg ggggaggctt agttcagcct 60  
 ggggggtccc tgagactctc ctgtgcagcc tctggattca cttcagtag ctactggatg 120  
 cactgggtcc gccaaagctcc agggaagggg ctggtgtggg tctcacgtat taatagtgat 180  
 gggagtagca caagctacgc ggactccgtg aagggccgat tcaccatctc cagagacaac 240  
 gccagaaca cgctgtatct gcaaataaac agtctgagag ccgaggacac ggctgtgtat 300  
 tactgtgcaa gagatccaac aggaggaagc tacataccta catttggaag aggaaccagc 360  
 cttattgttc atccg 375

<210> 34  
 <211> 125  
 <212> PRT  
 <213> Homo sapiens

<400> 34  
 Thr Gly Val Leu Ser Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu  
 1 5 10 15  
 Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr  
 20 25 30  
 Ser Ile Ser Ser Gly Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly  
 35 40 45  
 Lys Gly Leu Glu Trp Ile Gly Ser Ile Tyr His Ser Gly Ser Thr Tyr  
 50 55 60  
 Tyr Asn Pro Ser Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser  
 65 70 75 80  
 Lys Asn Gln Phe Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr  
 85 90 95  
 Ala Val Tyr Tyr Cys Ala Arg Val Arg Arg Arg Tyr Ser Ser Ala Ser  
 100 105 110  
 Lys Ile Ile Phe Gly Ser Gly Thr Arg Leu Ser Ile Arg  
 115 120 125

17/299

<210> 35  
 <211> 377  
 <212> DNA  
 <213> Homo sapiens

<400> 35  
 tcacaggggt cctgtcccag gtgcagctgc aggagtcggg cccaggactg gtgaagcctt 60  
 cggagaccct gtccctcacc tgcactgtct ctgggttactc catcagcagt ggttactact 120  
 ggggctggat ccggcagccc ccagggaagg ggctggagtg gattgggagt atctatcata 180  
 gtgggagcac ctactacaac ccgtccctca agagtcgagt caccatatca gtagacacgt 240  
 ccaagaacca gttctccctg aagctgagct ctgtgaccgc cgcagacacg gccgtgtatt 300  
 actgtgcgag agtccgtcgg aggtacagca gtgcttccaa gataatcttt ggatcaggga 360  
 ccagactcag catccgg 377

<210> 36  
 <211> 140  
 <212> PRT  
 <213> Homo sapiens

<400> 36  
 Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala Pro Arg Trp  
 1 5 10 15  
 Val Leu Ser Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys  
 20 25 30  
 Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile  
 35 40 45  
 Ser Ser Gly Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly  
 50 55 60  
 Leu Glu Trp Ile Gly Ser Ile Tyr His Ser Gly Ser Thr Tyr Tyr Asn  
 65 70 75 80  
 Pro Ser Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn  
 85 90 95  
 Gln Phe Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val  
 100 105 110  
 Tyr Tyr Cys Ala Arg Val Arg Arg Arg Tyr Ser Ser Ala Ser Lys Ile  
 115 120 125  
 Ile Phe Gly Ser Gly Thr Arg Leu Ser Ile Arg Pro  
 130 135 140

<210> 37  
 <211> 675  
 <212> DNA  
 <213> Homo sapiens

<400> 37  
 ccacccacat gcaaactctc acttaggcgc ccacaggaag ccacaacaca tttccttaaa 60  
 ttcaggtcca actcataagg gaaatgcttt ctgagagtca tggacctcct gtgcaagaac 120  
 atgaagcacc tgtgggtttt cctcctgctg gtggcagctc ccagatgtga gtgtctcagg 180



18/299

```

gatccagacg tgaagatatg ggaagtgcct ctgatcccag ggctcaccgt ggggtttttct 240
gttcacaggg gtcctgtccc aggtgcagct gcaggagtcg ggcccaggac tggatgaagcc 300
ttcggagacc ctgtccctca cctgcactgt ctctgggttac tccatcagca gtggttacta 360
ctggggctgg atccggcagc cccaggggaa ggggctggag tggattggga gtatctatca 420
tagtgggagc acctactaca acccgtcctt caagagtcga gtcaccatat cagtagacac 480
gtccaagaac cagttctccc tgaagctgag ctctgtgacc gccgcagaca cggccgtgta 540
ttactgtgcg agagtccgtc ggaggtacag cagtgccttc aagataatct ttggatcagg 600
gaccagactc agcatccggc caagtaagta gaatgaagca ggagagcaag ggaggacgga 660
caactatttc ttctt 675

```

&lt;210&gt; 38

&lt;211&gt; 158

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 38

```

Met Val Thr Gly Gly Val Leu Ser Gln Val Gln Leu Gln Glu Ser Gly
  1                      5                      10                      15

```

```

Pro Gly Leu Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val
                20                      25                      30

```

```

Ser Gly Tyr Ser Ile Ser Ser Gly Tyr Tyr Trp Gly Trp Ile Arg Gln
    35                      40                      45

```

```

Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly Ser Ile Tyr His Ser Gly
    50                      55                      60

```

```

Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser Arg Val Thr Ile Ser Val
    65                      70                      75                      80

```

```

Asp Thr Ser Lys Asn Gln Phe Ser Leu Lys Leu Ser Ser Val Thr Ala
                85                      90                      95

```

```

Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Val Arg Arg Arg Tyr Ser
    100                      105                      110

```

```

Ser Ala Ser Lys Ile Ile Phe Gly Ser Gly Thr Arg Leu Ser Ile Arg
    115                      120                      125

```

```

Pro Asn Ile Gln Asn Pro Asp Pro Ala Val Tyr Gln Leu Arg Asp Ser
    130                      135                      140

```

```

Lys Ser Ser Asp Lys Ser Val Cys Leu Phe Thr Asp Phe Asp
    145                      150                      155

```

&lt;210&gt; 39

&lt;211&gt; 508

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 39

```

tgtcctctga aaactcggga atttgtcact gaaatgggtga caggaggggt cctgtcccag 60
gtgcagctgc aggagtcggg cccaggactg gtgaagcctt cggagaccct gtccctcacc 120
tgcactgtct ctggttactc catcagcagt gggttactact ggggctggat ccggcagccc 180
ccaggggaagg ggctggagtg gattgggagt atctatcata gtgggagcac ctactacaac 240

```

19/299

```

ccgtccctca agagtcgagt caccatatca gtagacacgt ccaagaacca gttctccctg 300
aagctgagct ctgtgaccgc cgcagacacg gccgtgtatt actgtgcgag agtccgtcgg 360
aggtacagca gtgcttccaa gataatcttt ggatcaggga ccagactcag catccggcca 420
aatatccaga accctgaccc tgccgtgtac cagctgagag actctaaatc cagtgacaag 480
tctgtctgcc tattcaccga ttttgatt                               508

```

&lt;210&gt; 40

&lt;211&gt; 162

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 40

```

Met Ala Glu Ala Leu His Gly Lys Arg Val Leu Ser Gln Val Gln Leu
  1           5           10          15

Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr Leu Ser Leu
          20          25          30

Ala Cys Thr Val Ser Gly Tyr Ser Ile Ser Ser Gly Tyr Tyr Trp Gly
          35          40          45

Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly Ser Ile
          50          55          60

Tyr His Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser Arg Val
          65          70          75          80

Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu Lys Leu Ser
          85          90          95

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Val Arg
          100         105         110

Arg Arg Tyr Ser Ser Ala Ser Lys Ile Ile Phe Gly Ser Gly Thr Arg
          115         120         125

Leu Ser Ile Arg Pro Asn Ile Gln Asn Pro Asp Pro Ala Val Tyr Gln
          130         135         140

Leu Arg Asp Ser Lys Ser Ser Asp Lys Ser Val Cys Leu Phe Thr Asp
          145         150         155         160

Phe Asp

```

&lt;210&gt; 41

&lt;211&gt; 616

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 41

```

tgtcctctga aaactcggga atttgtcact gaaatgggtga caggagccta cagggtggcag 60
atgagaactc tcaacacagt tgtgttagaa gaaggatttc ctagagagac cctgactcaa 120
tgatgataca tggctgaagc attgcatgga aaacgggtcc tgtcccagggt gcagctgcag 180
gagtcggggc caggactggt gaagccttcg gagaccctgt ccctcgccctg cactgtctct 240
ggttactcca tcagcagtgg ttactactgg ggctggatcc ggcagccccc aggggaagggg 300
ctggagtgga ttgggagtat ctatcatagt gggagcacct actacaaccc gtccctcaag 360

```

20/299

```

agtcgagtca ccatatcagt agacacgtcc aagaaccagt tctccctgaa gctgagctct 420
gtgaccgccg cagacacggc cgtgtattac tgtgcgagag tccgtcggag gtacagcagt 480
gcttccaaga taatcttttg atcagggacc agactcagca tccggccaaa tatccagaac 540
cctgaccctg ccgtgtacca gctgagagac tctaaatcca gtgacaagtc tgtctgccta 600
ttcacccgatt ttgatt                                     616

```

&lt;210&gt; 42

&lt;211&gt; 550

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 42

```

Gly Tyr Gln Leu His Gly Ala Glu Val Asn Gly Gly Leu Pro Ser Ala
  1              5              10              15

Ser Ser Phe Ser Ser Ala Pro Gly Ala Thr Tyr Gly Val Ser Ser His
      20              25              30

Thr Pro Pro Val Ser Gly Ala Asp Ser Leu Leu Gly Ser Arg Gly Thr
      35              40              45

Thr Ala Gly Ser Ser Gly Asp Ala Leu Gly Lys Ala Leu Ala Ser Ile
      50              55              60

Tyr Ser Pro Asp His Ser Ser Asn Asn Phe Ser Ser Ser Pro Ser Thr
      65              70              75              80

Pro Val Gly Ser Pro Gln Gly Leu Ala Gly Thr Ser Gln Trp Pro Arg
      85              90              95

Ala Gly Ala Pro Gly Ala Leu Ser Pro Ser Tyr Asp Gly Gly Leu His
      100             105             110

Gly Leu Gln Ser Lys Ile Glu Asp His Leu Asp Glu Ala Ile His Val
      115             120             125

Leu Arg Ser His Ala Val Gly Thr Ala Gly Asp Met His Thr Leu Leu
      130             135             140

Pro Gly His Gly Ala Leu Ala Ser Gly Phe Thr Gly Pro Met Ser Leu
      145             150             155             160

Gly Gly Arg His Ala Gly Leu Val Gly Gly Ser His Pro Glu Asp Gly
      165             170             175

Leu Ala Gly Ser Thr Ser Leu Met His Asn His Ala Ala Leu Pro Ser
      180             185             190

Gln Pro Gly Thr Leu Pro Asp Leu Ser Arg Pro Pro Asp Ser Tyr Ser
      195             200             205

Val Leu Ser Ile Arg Gly Ala Gln Glu Glu Glu Pro Thr Asp Pro Gln
      210             215             220

Leu Met Arg Leu Asp Asn Met Leu Leu Ala Glu Gly Val Ala Gly Pro
      225             230             235             240

```

21/299

Glu	Lys	Gly	Gly	Gly	Ser	Ala	Ala	Ala	Ala	Ala	Ala	Ala	Ala	Ala	Ser	
				245					250					255		
Gly	Gly	Ala	Gly	Ser	Asp	Asn	Ser	Val	Glu	His	Ser	Asp	Tyr	Arg	Ala	
				260					265					270		
Lys	Leu	Ser	Gln	Ile	Arg	Gln	Ile	Tyr	His	Thr	Glu	Leu	Glu	Lys	Tyr	
				275					280					285		
Glu	Gln	Ala	Cys	Asn	Glu	Phe	Thr	Thr	His	Val	Met	Asn	Leu	Leu	Arg	
				290					295					300		
Glu	Gln	Ser	Arg	Thr	Arg	Pro	Ile	Ser	Pro	Lys	Glu	Ile	Glu	Arg	Met	
				305					310					315		
Val	Ser	Ile	Ile	His	Arg	Lys	Phe	Ser	Ser	Ile	Gln	Met	Gln	Leu	Lys	
				325					330					335		
Gln	Ser	Thr	Cys	Glu	Ala	Val	Met	Ile	Leu	Arg	Ser	Arg	Phe	Leu	Asp	
				340					345					350		
Ala	Arg	Arg	Lys	Arg	Arg	Asn	Phe	Asn	Lys	Gln	Ala	Thr	Glu	Ile	Leu	
				355					360					365		
Asn	Glu	Tyr	Phe	Tyr	Ser	His	Leu	Ser	Asn	Pro	Tyr	Pro	Ser	Glu	Glu	
				370					375					380		
Ala	Lys	Glu	Glu	Leu	Ala	Lys	Lys	Cys	Gly	Ile	Thr	Val	Ser	Gln	Val	
				385					390					395		
Ser	Asn	Trp	Phe	Gly	Asn	Lys	Arg	Ile	Arg	Tyr	Lys	Lys	Asn	Ile	Gly	
				405					410					415		
Lys	Phe	Gln	Glu	Glu	Ala	Asn	Ile	Tyr	Ala	Ala	Lys	Thr	Ala	Val	Thr	
				420					425					430		
Ala	Thr	Asn	Val	Ser	Ala	His	Gly	Ser	Gln	Ala	Asn	Ser	Pro	Ser	Thr	
				435					440					445		
Pro	Asn	Ser	Ala	Gly	Ser	Ser	Ser	Ser	Phe	Asn	Met	Ser	Asn	Ser	Gly	
				450					455					460		
Asp	Leu	Phe	Met	Ser	Val	Gln	Ser	Leu	Asn	Gly	Asp	Ser	Tyr	Gln	Gly	
				465					470					475		
Ala	Gln	Val	Gly	Ala	Asn	Val	Gln	Ser	Gln	Val	Asp	Thr	Leu	Arg	His	
				485					490					495		
Val	Ile	Ser	Gln	Thr	Gly	Gly	Tyr	Ser	Asp	Gly	Leu	Ala	Ala	Ser	Gln	
				500					505					510		
Met	Tyr	Ser	Pro	Gln	Gly	Ile	Ser	Ala	Asn	Gly	Gly	Trp	Gln	Asp	Ala	
				515					520					525		
Thr	Thr	Pro	Ser	Ser	Val	Thr	Ser	Pro	Thr	Glu	Gly	Pro	Gly	Ser	Val	
				530					535					540		
His	Ser	Asp	Thr	Ser	Asn											

22/299

545

550

<210> 43  
 <211> 2049  
 <212> DNA  
 <213> Homo sapiens

<400> 43  
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 tacgttttc 2049

<210> 44  
 <211> 574  
 <212> PRT  
 <213> Homo sapiens

<400> 44  
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 Ser Asp Leu Leu Asp Phe Ser Met Met Phe Pro Leu Pro Val Thr Asn  
 20 25 30

23/299

Gly Lys Gly Arg Pro Ala Ser Leu Ala Gly Ala Gln Phe Gly Gly Ser  
           35                                  40                                  45  
 Gly Leu Glu Asp Arg Pro Ser Ser Gly Ser Trp Gly Ser Gly Asp Gln  
           50                                  55                                  60  
 Ser Ser Ser Ser Phe Asp Pro Ser Arg Thr Phe Ser Glu Gly Thr His  
       65                                  70                                  75                                  80  
 Phe Thr Glu Ser His Ser Ser Leu Ser Ser Thr Phe Leu Gly Pro  
                                   85                                  90                                  95  
 Gly Leu Gly Gly Lys Ser Gly Glu Arg Gly Ala Tyr Ala Ser Phe Gly  
                                   100                                  105                                  110  
 Arg Asp Ala Gly Val Gly Gly Leu Thr Gln Ala Gly Phe Leu Ser Gly  
           115                                  120                                  125  
 Glu Leu Ala Leu Asn Ser Pro Gly Pro Leu Ser Pro Ser Gly Met Lys  
           130                                  135                                  140  
 Gly Thr Ser Gln Tyr Tyr Pro Ser Tyr Ser Gly Ser Ser Arg Arg Arg  
   145                                  150                                  155                                  160  
 Ala Ala Asp Gly Ser Leu Asp Thr Gln Pro Lys Lys Val Arg Lys Val  
                                   165                                  170                                  175  
 Pro Pro Gly Leu Pro Ser Ser Val Tyr Pro Pro Ser Ser Gly Glu Asp  
                                   180                                  185                                  190  
 Tyr Gly Arg Asp Ala Thr Ala Tyr Pro Ser Ala Lys Thr Pro Ser Ser  
       195                                  200                                  205  
 Thr Tyr Pro Ala Pro Phe Tyr Val Ala Asp Gly Ser Leu His Pro Ser  
       210                                  215                                  220  
 Ala Glu Leu Trp Ser Pro Pro Gly Gln Ala Gly Phe Gly Pro Met Leu  
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 Gly Gly Gly Ser Ser Pro Leu Pro Leu Pro Pro Gly Ser Gly Pro Val  
                                   245                                  250                                  255  
 Gly Ser Ser Gly Ser Ser Ser Thr Phe Gly Gly Leu His Gln His Glu  
                                   260                                  265                                  270  
 Arg Met Gly Tyr Gln Leu His Gly Ala Glu Val Asn Gly Gly Leu Pro  
       275                                  280                                  285  
 Ser Ala Ser Ser Phe Ser Ser Ala Pro Gly Ala Thr Tyr Gly Gly Val  
       290                                  295                                  300  
 Ser Ser His Thr Pro Pro Val Ser Gly Ala Asp Ser Leu Leu Gly Ser  
   305                                  310                                  315                                  320  
 Arg Gly Thr Thr Ala Gly Ser Ser Gly Asp Ala Leu Gly Lys Ala Leu  
                                   325                                  330                                  335  
 Ala Ser Ile Tyr Ser Pro Asp His Ser Ser Asn Asn Phe Ser Ser Ser

24/299

340	345	350
Pro Ser Thr Pro Val Gly Ser Pro Gln Gly Leu Ala Gly Thr Ser Gln		
355	360	365
Trp Pro Arg Ala Gly Ala Pro Gly Ala Leu Ser Pro Ser Tyr Asp Gly		
370	375	380
Gly Leu His Gly Leu Gln Ser Lys Ile Glu Asp His Leu Asp Glu Ala		
385	390	395
Ile His Val Leu Arg Ser His Ala Val Gly Thr Ala Gly Asp Met His		
405	410	415
Thr Leu Leu Pro Gly His Gly Ala Leu Ala Ser Gly Phe Thr Ser Pro		
420	425	430
Met Ser Leu Gly Gly Arg His Ala Gly Leu Val Gly Gly Ser His Pro		
435	440	445
Glu Asp Gly Leu Ala Gly Ser Thr Ser Leu Met His Asn His Ala Ala		
450	455	460
Leu Pro Ser Gln Pro Gly Thr Leu Pro Asp Leu Ser Arg Pro Pro Asp		
465	470	475
Ser Tyr Ser Gly Gln Gly Ile Ser Pro Gln Leu Gly Pro Leu Ser Thr		
485	490	495
Ser Ile Tyr Leu Leu Thr Gln Asp Asp Lys Tyr Trp Ala Arg Arg Arg		
500	505	510
Lys Asn Asn Met Ala Ala Lys Arg Ser Arg Asp Ala Arg Arg Leu Lys		
515	520	525
Glu Asn Gln Ile Ala Ile Arg Ala Ser Phe Leu Glu Lys Glu Asn Ser		
530	535	540
Ala Leu Arg Gln Glu Val Ala Asp Leu Arg Lys Glu Leu Gly Lys Cys		
545	550	555
Lys Asn Ile Leu Ala Lys Tyr Glu Ala Arg His Gly Pro Leu		
565	570	

&lt;210&gt; 45

&lt;211&gt; 4410

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 45

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26/299

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gaaaaaaata aaaagattct aataaaaaaa 4410

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&lt;210&gt; 46

&lt;211&gt; 416

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 46

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Pro Asn Ser Asn His Val Ala Ser Gly Ala Gly Glu Ala Ala Ile Glu
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Thr Gln Ser Ser Ser Ser Glu Glu Ile Val Pro Ser Pro Pro Ser Pro
                20                      25                      30

Pro Pro Leu Pro Arg Ile Tyr Lys Pro Cys Phe Val Cys Gln Asp Lys
                35                      40                      45

Ser Ser Gly Tyr His Tyr Gly Val Ser Ala Cys Glu Gly Cys Lys Gly
  50                      55                      60

Phe Phe Arg Arg Ser Ile Gln Lys Asn Met Val Tyr Thr Cys His Arg
  65                      70                      75                      80

Asp Lys Asn Cys Ile Ile Asn Lys Val Thr Arg Asn Arg Cys Gln Tyr
                85                      90                      95

Cys Arg Leu Gln Lys Cys Phe Glu Val Gly Met Ser Lys Glu Ser Val
                100                      105                      110

Arg Asn Asp Arg Asn Lys Lys Lys Lys Glu Val Pro Lys Pro Glu Cys
  115                      120                      125

Ser Glu Ser Tyr Thr Leu Thr Pro Glu Val Gly Glu Leu Ile Glu Lys
  130                      135                      140

Val Arg Lys Ala His Gln Glu Thr Phe Pro Ala Leu Cys Gln Leu Gly
  145                      150                      155                      160

Lys Tyr Thr Thr Asn Asn Ser Ser Glu Gln Arg Val Ser Leu Asp Ile
                165                      170                      175

Asp Leu Trp Asp Lys Phe Ser Glu Leu Ser Thr Lys Cys Ile Ile Lys
  180                      185                      190

Thr Val Glu Phe Ala Lys Gln Leu Pro Gly Phe Thr Thr Leu Thr Ile
  195                      200                      205

Ala Asp Gln Ile Thr Leu Leu Lys Ala Ala Cys Leu Asp Ile Leu Ile
  210                      215                      220

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27/299

Leu Arg Ile Cys Thr Arg Tyr Thr Pro Glu Gln Asp Thr Met Thr Phe  
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 Ser Asp Gly Leu Thr Leu Asn Arg Thr Gln Met His Asn Ala Gly Phe  
 245 250 255  
 Gly Pro Leu Thr Asp Leu Val Phe Ala Phe Ala Asn Gln Leu Leu Pro  
 260 265 270  
 Leu Glu Met Asp Asp Ala Glu Thr Gly Leu Leu Ser Ala Ile Cys Leu  
 275 280 285  
 Ile Cys Gly Asp Arg Gln Asp Leu Glu Gln Pro Asp Arg Val Asp Met  
 290 295 300  
 Leu Gln Glu Pro Leu Leu Glu Ala Leu Lys Val Tyr Val Arg Lys Arg  
 305 310 315 320  
 Arg Pro Ser Arg Pro His Met Phe Pro Lys Met Leu Met Lys Ile Thr  
 325 330 335  
 Asp Leu Arg Ser Ile Ser Ala Lys Gly Ala Glu Arg Val Ile Thr Leu  
 340 345 350  
 Lys Met Glu Ile Pro Gly Ser Met Pro Pro Leu Ile Gln Glu Met Leu  
 355 360 365  
 Glu Asn Ser Glu Gly Leu Asp Thr Leu Ser Gly Gln Pro Gly Gly Gly  
 370 375 380  
 Gly Arg Asp Gly Gly Gly Leu Ala Pro Pro Pro Gly Ser Cys Ser Pro  
 385 390 395 400  
 Ser Leu Ser Pro Ser Ser Asn Arg Ser Ser Pro Ala Thr His Ser Pro  
 405 410 415

&lt;210&gt; 47

&lt;211&gt; 1284

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 47

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28/299

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&lt;210&gt; 48

&lt;211&gt; 797

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 48

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Met Glu Pro Ala Pro Ala Arg Ser Pro Arg Pro Gln Gln Asp Pro Ala
  1                      5                      10                      15

Arg Pro Gln Glu Pro Thr Met Pro Pro Pro Glu Thr Pro Ser Glu Gly
                20                      25                      30

Arg Gln Pro Ser Pro Ser Pro Ser Pro Thr Glu Arg Ala Pro Ala Ser
        35                      40                      45

Glu Glu Glu Phe Gln Phe Leu Arg Cys Gln Gln Cys Gln Ala Glu Ala
  50                      55                      60

Lys Cys Pro Lys Leu Leu Pro Cys Leu His Thr Leu Cys Ser Gly Cys
  65                      70                      75                      80

Leu Glu Ala Ser Gly Met Gln Cys Pro Ile Cys Gln Ala Pro Trp Pro
                85                      90                      95

Leu Gly Ala Asp Thr Pro Ala Leu Asp Asn Val Phe Phe Glu Ser Leu
        100                      105                      110

Gln Arg Arg Leu Ser Val Tyr Arg Gln Ile Val Asp Ala Gln Ala Val
        115                      120                      125

Cys Thr Arg Cys Lys Glu Ser Ala Asp Phe Trp Cys Phe Glu Cys Glu
        130                      135                      140

Gln Leu Leu Cys Ala Lys Cys Phe Glu Ala His Gln Trp Phe Leu Lys
        145                      150                      155                      160

His Glu Ala Arg Pro Leu Ala Glu Leu Arg Asn Gln Ser Val Arg Glu
                165                      170                      175

Phe Leu Asp Gly Thr Arg Lys Thr Asn Asn Ile Phe Cys Ser Asn Pro
        180                      185                      190

Asn His Arg Thr Pro Thr Leu Thr Ser Ile Tyr Cys Arg Gly Cys Ser
        195                      200                      205

Lys Pro Leu Cys Cys Ser Cys Ala Leu Leu Asp Ser Ser His Ser Glu
        210                      215                      220

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29/299

Leu	Lys	Cys	Asp	Ile	Ser	Ala	Glu	Ile	Gln	Gln	Arg	Gln	Glu	Glu	Leu	225	230	235	240
Asp	Ala	Met	Thr	Gln	Ala	Leu	Gln	Glu	Gln	Asp	Ser	Ala	Phe	Gly	Ala	245	250	255	
Val	His	Ala	Gln	Met	His	Ala	Ala	Val	Gly	Gln	Leu	Gly	Arg	Ala	Arg	260	265	270	
Ala	Glu	Thr	Glu	Glu	Leu	Ile	Arg	Glu	Arg	Val	Arg	Gln	Val	Val	Ala	275	280	285	
His	Val	Arg	Ala	Gln	Glu	Arg	Glu	Leu	Leu	Glu	Ala	Val	Asp	Ala	Arg	290	295	300	
Tyr	Gln	Arg	Asp	Tyr	Glu	Glu	Met	Ala	Ser	Arg	Leu	Gly	Arg	Leu	Asp	305	310	315	320
Ala	Val	Leu	Gln	Arg	Ile	Arg	Thr	Gly	Ser	Ala	Leu	Val	Gln	Arg	Met	325	330	335	
Lys	Cys	Tyr	Ala	Ser	Asp	Gln	Glu	Val	Leu	Asp	Met	His	Gly	Phe	Leu	340	345	350	
Arg	Gln	Ala	Leu	Cys	Arg	Leu	Arg	Gln	Glu	Glu	Pro	Gln	Ser	Leu	Gln	355	360	365	
Ala	Ala	Val	Arg	Thr	Asp	Gly	Phe	Asp	Glu	Phe	Lys	Val	Arg	Leu	Gln	370	375	380	
Asp	Leu	Ser	Ser	Cys	Ile	Thr	Gln	Gly	Lys	Ala	Ile	Glu	Thr	Gln	Ser	385	390	395	400
Ser	Ser	Ser	Glu	Glu	Ile	Val	Pro	Ser	Pro	Pro	Ser	Pro	Pro	Pro	Leu	405	410	415	
Pro	Arg	Ile	Tyr	Lys	Pro	Cys	Phe	Val	Cys	Gln	Asp	Lys	Ser	Ser	Gly	420	425	430	
Tyr	His	Tyr	Gly	Val	Ser	Ala	Cys	Glu	Gly	Cys	Lys	Gly	Phe	Phe	Arg	435	440	445	
Arg	Ser	Ile	Gln	Lys	Asn	Met	Val	Tyr	Thr	Cys	His	Arg	Asp	Lys	Asn	450	455	460	
Cys	Ile	Ile	Asn	Lys	Val	Thr	Arg	Asn	Arg	Cys	Gln	Tyr	Cys	Arg	Leu	465	470	475	480
Gln	Lys	Cys	Phe	Glu	Val	Gly	Met	Ser	Lys	Glu	Ser	Val	Arg	Asn	Asp	485	490	495	
Arg	Asn	Lys	Lys	Lys	Lys	Glu	Val	Pro	Lys	Pro	Glu	Cys	Ser	Glu	Ser	500	505	510	
Tyr	Thr	Leu	Thr	Pro	Glu	Val	Gly	Glu	Leu	Ile	Glu	Lys	Val	Arg	Lys	515	520	525	
Ala	His	Gln	Glu	Thr	Phe	Pro	Ala	Leu	Cys	Gln	Leu	Gly	Lys	Tyr	Thr				

530					535					540					
Thr 545	Asn	Asn	Ser	Ser	Glu 550	Gln	Arg	Val	Ser	Leu 555	Asp	Ile	Asp	Leu	Trp 560
Asp	Lys	Phe	Ser	Glu 565	Leu	Ser	Thr	Lys	Cys 570	Ile	Ile	Lys	Thr	Val 575	Glu
Phe	Ala	Lys	Gln 580	Leu	Pro	Gly	Phe	Thr 585	Thr	Leu	Thr	Ile	Ala 590	Asp	Gln
Ile	Thr	Leu 595	Leu	Lys	Ala	Ala	Cys 600	Leu	Asp	Ile	Leu	Ile 605	Leu	Arg	Ile
Cys 610	Thr	Arg	Tyr	Thr	Pro	Glu 615	Gln	Asp'	Thr	Met	Thr 620	Phe	Ser	Asp	Gly
Leu 625	Thr	Leu	Asn	Arg	Thr 630	Gln	Met	His	Asn	Ala 635	Gly	Phe	Gly	Pro	Leu 640
Thr	Asp	Leu	Val	Phe 645	Ala	Phe	Ala	Asn	Gln 650	Leu	Leu	Pro	Leu	Glu 655	Met
Asp	Asp	Ala	Glu 660	Thr	Gly	Leu	Leu	Ser 665	Ala	Ile	Cys	Leu	Ile 670	Cys	Gly
Asp	Arg	Gln 675	Asp	Leu	Glu	Gln	Pro 680	Asp	Arg	Val	Asp 685	Met	Leu	Gln	Glu
Pro 690	Leu	Leu	Glu	Ala	Leu	Lys 695	Val	Tyr	Val	Arg	Lys 700	Arg	Arg	Pro	Ser
Arg 705	Pro	His	Met	Phe	Pro 710	Lys	Met	Leu	Met	Lys 715	Ile	Thr	Asp	Leu	Arg 720
Ser	Ile	Ser	Ala	Lys 725	Gly	Ala	Glu	Arg	Val 730	Ile	Thr	Leu	Lys	Met 735	Glu
Ile	Pro	Gly 740	Ser	Met	Pro	Pro	Leu	Ile 745	Gln	Glu	Met	Leu	Glu 750	Asn	Ser
Glu	Gly	Leu 755	Asp	Thr	Leu	Ser	Gly 760	Gln	Pro	Gly	Gly 765	Gly	Gly	Arg	Asp
Gly 770	Gly	Gly	Leu	Ala	Pro	Pro 775	Pro	Gly	Ser	Cys	Ser 780	Pro	Ser	Leu	Ser
Pro 785	Ser	Ser	Asn	Arg	Ser 790	Ser	Pro	Ala	Thr	His 795	Ser	Pro			

ctccccttca gcttctcttc acgcactcca agatctaaac cgagaatcga aactaagctg 60

31/299

gggtccatgg agcctgcacc cgcccgatct ccgaggcccc agcaggaccc cgcccggccc 120  
caggagcccc ccctgcctcc ccccgagacc ccctctgaag gccgccagcc cagccccagc 180  
cccagcccta cagagcgagc ccccgcttcg gaggaggagt tccagtttct gcgctgccag 240  
caatgccagg cggaagccaa gtgcccgaag ctgctgcctt gtctgcacac gctgtgctca 300  
ggatgcctgg aggcgtcggg catgcagtgc cccatctgcc aggcgccttg gcccttaggt 360  
gcagacacac ccgccctgga taacgtcttt ttcgagagtc tgcagcggcg cctgtcggtg 420  
taccggcaga ttgtggatgc gcaggctgtg tgcacccgct gcaaagagtc ggccgacttc 480  
tggtgctttg agtgcgagca gctcctctgc gccaaagtgt tgcaggcaca ccagtggttc 540  
ctcaagcacg aggcgccggcc cctagcagag ctgcgcacac agtcgggtgc tgagttcctg 600  
gacggcaccg gcaagaccaa caacatcttc tgctccaacc ccaaccaccg caccctacg 660  
ctgaccagca tctactgccg aggatgttcc aagccgctgt gctgctcgtg cgcgctcctt 720  
gacagcagcc acagtgcagt caagtgcgac atcagcgag agatccagca gcgacaggag 780  
gagctggacg ccattgacgca ggcgctgcag gacgaggata gtgcctttgg cgcggttcac 840  
gcgcagatgc acgcggccgt cgccagctg ggccgcgcgc gtgcccagac cgaggagctg 900  
atccgcgagc gcgtgcgcca ggtggtagct cacgtgcggg ctgaggagcg cgagctgctg 960  
gaggctgtgg acgcgcgcta ccagcgcgac tacgaggaga tggccagtcg gctgggcccg 1020  
ctggatgctg tgctgcagcg catccgcacg ggcagcgcgc tgggtgcagag gatgaagtgc 1080  
tacgcctcgg accaggaggt gctggacatg cacggtttcc tgcgccaggc gctctgccgc 1140  
ctgcgccagg aggagcccca gagcctgcaa gctgccgtgc gcaccgatgg cttcgacgag 1200  
ttcaagggtg gcctgcagga cctcagctct tgcatcacc aggggaaagc cattgagacc 1260  
cagacagca gttctgaaga gatagtgcct agcctccct cgccaccccc tctaccccgc 1320  
atctacaagc cttgctttgt ctgtcaggac aagtcctcag gctaccacta tggggtcagc 1380  
gcctgtgagg gctgcaaggg cttcttccgc cgcagcatcc agaagaacat ggtgtacacg 1440  
tgtcaccggg acaagaactg catcatcaac aaggtgaccc ggaaccgctg ccagtactgc 1500  
cgactgcaga agtgctttga agtgggcatg tccaaggagt ctgtgagaaa cgaccgaaac 1560  
aagaagaaga aggaggtgcc caagcccagag tgctctgaga gctacacgct gacgcggag 1620  
gtgggggagc tcattgagaa ggtgcgcaaa gcgcaccagg aaaccttccc tgccctctgc 1680  
cagctgggca aatacactac gaacaacagc tcagaacaac gtgtctctct ggacattgac 1740  
ctctgggaca agttcagtga actctccacc aagtgcatca ttaagactgt ggagttcgcc 1800  
aagcagctgc ccggcttcac caccctcacc atcgccgacc agatcacccct cctcaaggct 1860  
gcctgcctg acatcctgat cctgcggatc tgcacgcggt acacgcccga gcaggacacc 1920  
atgaccttct cggacgggct gaccctgaac cggaccaga tgcacaacgc tggcttcggc 1980  
ccccacccg acctggctct tgcttctgcc aaccagctgc tgcccctgga gatggatgat 2040  
gcggagacgg ggctgctcag cgccatctgc ctcatctgcg gagaccgcca ggacctggag 2100  
cagccggacc ggggtggacat gctgcaggag ccgctgctgg aggcgctaaa ggtctacgtg 2160  
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ctgcgaagca tcagcgccaa gggggctgag cgggtgatca cgctgaagat ggagatcccg 2280  
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tgtagcccca gcctcagccc cagctccaac agaagcagcc cggccaccca ctcccgtga 2460  
ccgccacgc cacatggaca cagccctcgc cctccgcccc ggcttttctc tgcccttcta 2520  
ccgacctgt gaccccgcac cagccctgcc cccacctgcc ctcccgggca gtactgggga 2580  
ccttccctgg gggacgggga gggaggaggc agcgactcct tggacagagg cctgggccct 2640  
cagtggactg cctgctccca cagcctgggc tgacgtcaga ggccgaggcc aggaactgag 2700  
tgaggccccct ggtcctgggt ctcaggatgg gtccctgggg cctcgtgttc atcaagacac 2760  
ccctctgccc agctcaccac atcttcatca ccagcaaacg ccaggacttg gctcccccat 2820  
cctcagaact cacaagccat tgctccccag ctggggaacc tcaacctccc ccctgcctcg 2880  
gttggtgaca gagggggtgg gacaggggcg ggggggtccc cctgtacata ccctgccata 2940  
ccaaccccag gtattaatc tcgctgggtt tgtttttatt ttaatttttt tgttttgatt 3000  
tttttaataa gaattttcat tttaagcaaa aaaaaa 3036

&lt;210&gt; 50

&lt;211&gt; 99

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 50

32/299

Asp Val Ser Asn Thr Thr Thr Ala Gln Lys Arg Lys Cys Ser Gln Thr  
 1 5 10 15  
 Gln Cys Pro Arg Lys Val Ile Lys Met Glu Ser Glu Glu Gly Lys Glu  
 20 25 30  
 Ala Arg Leu Ala Leu Pro Ala Pro Gly Pro Tyr Ser Thr Pro Leu Arg  
 35 40 45  
 Thr Pro Leu Trp Asn Gly Ser Asn His Ser Ile Glu Thr Gln Ser Ser  
 50 55 60  
 Ser Ser Glu Glu Ile Val Pro Ser Pro Pro Ser Pro Pro Pro Leu Pro  
 65 70 75 80  
 Arg Ile Tyr Lys Pro Cys Phe Val Cys Gln Asp Lys Ser Ser Gly Tyr  
 85 90 95  
 His Tyr Gly

<210> 51  
 <211> 296  
 <212> DNA  
 <213> Homo sapiens

<400> 51  
 gatgtctcca atacaacgac agcccagaag aggaagtgca gccagaccca gtgccccagg 60  
 aaggtcatca agatggagtc tgaggagggg aaggaggcaa gggtggctct ccccgccccg 120  
 ggtccgtact ccaccccgct ccggactccg ctttggaatg gctcaaacca ctccattgag 180  
 acccagagca gcagttctga agagatagtg cccagccctc cctcgccacc cctcttacct 240  
 cgcatttaca agccttgctt tgtctgtcag gacaagtcct caggctacca ctatgg 296

<210> 52  
 <211> 858  
 <212> PRT  
 <213> Homo sapiens

<400> 52  
 Met Asp Leu Thr Lys Met Gly Met Ile Gln Leu Gln Asn Pro Ser His  
 1 5 10 15  
 Pro Thr Gly Leu Leu Cys Lys Ala Asn Gln Met Arg Leu Ala Gly Thr  
 20 25 30  
 Leu Cys Asp Val Val Ile Met Val Asp Ser Gln Glu Phe His Ala His  
 35 40 45  
 Arg Thr Val Leu Ala Cys Thr Ser Lys Met Phe Glu Ile Leu Phe His  
 50 55 60  
 Arg Asn Ser Gln His Tyr Thr Leu Asp Phe Leu Ser Pro Lys Thr Phe  
 65 70 75 80  
 Gln Gln Ile Leu Glu Tyr Ala Tyr Thr Ala Thr Leu Gln Ala Lys Ala  
 85 90 95

33/299

Glu Asp Leu Asp Asp Leu Leu Tyr Ala Ala Glu Ile Leu Glu Ile Glu  
 100 105 110  
 Tyr Leu Glu Glu Gln Cys Leu Lys Met Leu Glu Thr Ile Gln Ala Ser  
 115 120 125  
 Asp Asp Asn Asp Thr Glu Ala Thr Met Ala Asp Gly Gly Ala Glu Glu  
 130 135 140  
 Glu Glu Asp Arg Lys Ala Arg Tyr Leu Lys Asn Ile Phe Ile Ser Lys  
 145 150 155 160  
 His Ser Ser Glu Glu Ser Gly Tyr Ala Ser Val Ala Gly Gln Ser Leu  
 165 170 175  
 Pro Gly Pro Met Val Asp Gln Ser Pro Ser Val Ser Thr Ser Phe Gly  
 180 185 190  
 Leu Ser Ala Met Ser Pro Thr Lys Ala Ala Val Asp Ser Leu Met Thr  
 195 200 205  
 Ile Gly Gln Ser Leu Leu Gln Gly Thr Leu Gln Pro Pro Ala Gly Pro  
 210 215 220  
 Glu Glu Pro Thr Leu Ala Gly Gly Gly Arg His Pro Gly Val Ala Glu  
 225 230 235 240  
 Val Lys Thr Glu Met Met Gln Val Asp Glu Val Pro Ser Gln Asp Ser  
 245 250 255  
 Pro Gly Ala Ala Glu Ser Ser Ile Ser Gly Gly Met Gly Asp Lys Val  
 260 265 270  
 Glu Glu Arg Gly Lys Glu Gly Pro Gly Thr Pro Thr Arg Ser Ser Val  
 275 280 285  
 Ile Thr Ser Ala Arg Glu Leu His Tyr Gly Arg Glu Glu Ser Ala Glu  
 290 295 300  
 Gln Val Pro Pro Pro Ala Glu Ala Gly Gln Ala Pro Thr Gly Arg Pro  
 305 310 315 320  
 Glu His Pro Ala Pro Pro Pro Glu Lys His Leu Gly Ile Tyr Ser Val  
 325 330 335  
 Leu Pro Asn His Lys Ala Asp Ala Val Leu Ser Met Pro Ser Ser Val  
 340 345 350  
 Thr Ser Gly Leu His Val Gln Pro Ala Leu Ala Val Ser Met Asp Phe  
 355 360 365  
 Ser Thr Tyr Gly Gly Leu Leu Pro Gln Gly Phe Ile Gln Arg Glu Leu  
 370 375 380  
 Phe Ser Lys Leu Gly Glu Leu Ala Val Gly Met Lys Ser Glu Ser Arg  
 385 390 395 400  
 Thr Ile Gly Glu Gln Cys Ser Val Cys Gly Val Glu Leu Pro Asp Asn



34/299

405					410					415					
Glu	Ala	Val	Glu	Gln	His	Arg	Lys	Leu	His	Ser	Gly	Met	Lys	Thr	Tyr
			420					425					430		
Gly	Cys	Glu	Leu	Cys	Gly	Lys	Arg	Phe	Leu	Asp	Ser	Leu	Arg	Leu	Arg
		435					440					445			
Met	His	Leu	Leu	Ala	His	Ser	Ala	Ile	Glu	Thr	Gln	Ser	Ser	Ser	Ser
	450					455					460				
Glu	Glu	Ile	Val	Pro	Ser	Pro	Pro	Ser	Pro	Pro	Pro	Leu	Pro	Arg	Ile
465					470					475					480
Tyr	Lys	Pro	Cys	Phe	Val	Cys	Gln	Asp	Lys	Ser	Ser	Gly	Tyr	His	Tyr
				485					490					495	
Gly	Val	Ser	Ala	Cys	Glu	Gly	Cys	Lys	Gly	Phe	Phe	Arg	Arg	Ser	Ile
			500					505					510		
Gln	Lys	Asn	Met	Val	Tyr	Thr	Cys	His	Arg	Asp	Lys	Asn	Cys	Ile	Ile
		515					520					525			
Asn	Lys	Val	Thr	Arg	Asn	Arg	Cys	Gln	Tyr	Cys	Arg	Leu	Gln	Lys	Cys
	530					535					540				
Phe	Glu	Val	Gly	Met	Ser	Lys	Glu	Ser	Val	Arg	Asn	Asp	Arg	Asn	Lys
545					550					555					560
Lys	Lys	Lys	Glu	Val	Pro	Lys	Pro	Glu	Cys	Ser	Glu	Ser	Tyr	Thr	Leu
			565						570					575	
Thr	Pro	Glu	Val	Gly	Glu	Leu	Ile	Glu	Lys	Val	Arg	Lys	Ala	His	Gln
			580					585					590		
Glu	Thr	Phe	Pro	Ala	Leu	Cys	Gln	Leu	Gly	Lys	Tyr	Thr	Thr	Asn	Asn
		595					600					605			
Ser	Ser	Glu	Gln	Arg	Val	Ser	Leu	Asp	Ile	Asp	Leu	Trp	Asp	Lys	Phe
	610					615					620				
Ser	Glu	Leu	Ser	Thr	Lys	Cys	Ile	Ile	Lys	Thr	Val	Glu	Phe	Ala	Lys
625					630					635					640
Gln	Leu	Pro	Gly	Phe	Thr	Thr	Leu	Thr	Ile	Ala	Asp	Gln	Ile	Thr	Leu
			645						650					655	
Leu	Lys	Ala	Ala	Cys	Leu	Asp	Ile	Leu	Ile	Leu	Arg	Ile	Cys	Thr	Arg
			660					665					670		
Tyr	Thr	Pro	Glu	Gln	Asp	Thr	Met	Thr	Phe	Ser	Asp	Gly	Leu	Thr	Leu
		675					680					685			
Asn	Arg	Thr	Gln	Met	His	Met	Ala	Gly	Phe	Gly	Pro	Leu	Thr	Asp	Leu
	690					695					700				
Val	Phe	Ala	Phe	Ala	Asn	Gln	Leu	Leu	Pro	Leu	Glu	Met	Asp	Asp	Ala
705					710					715					720

35/299

Glu Thr Gly Leu Leu Ser Ala Ile Cys Leu Ile Cys Gly Asp Arg Gln  
                     725                    730                    735  
 Asp Leu Glu Gln Pro Asp Arg Val Asp Met Leu Gln Glu Pro Leu Leu  
                     740                    745                    750  
 Glu Ala Leu Lys Val Tyr Val Arg Lys Arg Arg Pro Ser Arg Pro His  
                     755                    760                    765  
 Met Phe Pro Lys Met Leu Met Lys Ile Thr Asp Leu Arg Ser Ile Ser  
                     770                    775                    780  
 Ala Lys Gly Ala Glu Arg Val Ile Thr Leu Lys Met Glu Ile Pro Gly  
                     785                    790                    795                    800  
 Ser Met Pro Pro Leu Ile Gln Glu Met Leu Glu Asn Ser Glu Gly Leu  
                     805                    810                    815  
 Asp Thr Leu Ser Gly Gln Pro Gly Gly Gly Gly Arg Asp Gly Gly Gly  
                     820                    825                    830  
 Leu Ala Pro Pro Pro Gly Ser Cys Ser Pro Ser Leu Ser Pro Ser Ser  
                     835                    840                    845  
 Asn Arg Ser Ser Pro Ala Thr His Ser Pro  
                     850                    855

&lt;210&gt; 53

&lt;211&gt; 277

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 53

Met Ala Ser Asn Ser Ser Ser Cys Pro Thr Pro Gly Gly Gly His Leu  
   1                    5                    10                    15  
 Asn Gly Tyr Pro Val Pro Pro Tyr Ala Phe Phe Phe Pro Pro Met Leu  
                     20                    25                    30  
 Gly Gly Leu Ser Pro Pro Gly Ala Leu Thr Thr Leu Gln His Gln Leu  
                     35                    40                    45  
 Pro Val Ser Gly Tyr Ser Thr Pro Ser Pro Ala Thr Gly Ala Lys Ala  
                     50                    55                    60  
 Phe Val Cys Asp Gln Cys Gly Ala Gln Phe Ser Lys Glu Asp Ala Leu  
   65                    70                    75                    80  
 Glu Thr His Arg Gln Thr His Thr Gly Thr Asp Met Ala Val Phe Cys  
                     85                    90                    95  
 Leu Leu Cys Gly Lys Arg Phe Gln Ala Gln Ser Ala Leu Gln Gln His  
                     100                    105                    110  
 Met Glu Val His Ala Gly Val Arg Ser Tyr Ile Cys Ser Glu Cys Asn  
                     115                    120                    125

36/299

Arg Thr Phe Pro Ser His Thr Ala Leu Lys Arg His Leu Arg Ser His  
 130 135 140  
 Thr Gly Asp His Pro Tyr Glu Cys Glu Phe Cys Gly Ser Cys Phe Arg  
 145 150 155 160  
 Asp Glu Ser Thr Leu Lys Ser His Lys Arg Ile His Thr Gly Glu Lys  
 165 170 175  
 Pro Tyr Glu Cys Asn Gly Cys Asp Lys Lys Phe Ser Leu Lys His Gln  
 180 185 190  
 Leu Glu Thr His Tyr Arg Val His Thr Gly Glu Lys Pro Phe Glu Cys  
 195 200 205  
 Lys Leu Cys His Gln Arg Ser Arg Asp Tyr Ser Ala Met Ile Lys His  
 210 215 220  
 Leu Arg Thr His Asn Gly Ala Ser Pro Tyr Gln Cys Thr Ile Cys Thr  
 225 230 235 240  
 Glu Tyr Cys Pro Ser Leu Ser Ser Met Gln Lys His Met Lys Gly His  
 245 250 255  
 Lys Pro Glu Glu Ile Pro Pro Asp Trp Arg Ile Glu Lys Thr Tyr Leu  
 260 265 270  
 Tyr Leu Cys Tyr Val  
 275

&lt;210&gt; 54

&lt;211&gt; 2311

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 54

Met Ala His Ser Cys Arg Trp Arg Phe Pro Ala Arg Pro Gly Thr Thr  
 1 5 10 15  
 Gly Gly Gly Gly Gly Gly Gly Arg Arg Gly Leu Gly Gly Gly Pro Arg  
 20 25 30  
 Gln Arg Val Pro Ala Leu Leu Leu Pro Pro Gly Pro Pro Val Gly Gly  
 35 40 45  
 Gly Gly Pro Gly Ala Pro Pro Ser Pro Pro Ala Val Ala Ala Ala  
 50 55 60  
 Ala Ala Ala Gly Ser Ser Gly Ala Gly Val Pro Gly Gly Ala Ala Ala  
 65 70 75 80  
 Ala Ser Ala Ala Ser Ser Ser Ser Ala Ser Ser Ser Ser Ser Ser  
 85 90 95  
 Ser Ser Ala Ser Ser Gly Pro Ala Leu Leu Arg Val Gly Pro Gly Phe  
 100 105 110

37/299

Asp	Ala	Ala	Leu	Gln	Val	Ser	Ala	Ala	Ile	Gly	Thr	Asn	Leu	Arg	Arg	115	120	125
Phe	Arg	Ala	Val	Phe	Gly	Glu	Ser	Gly	Gly	Gly	Gly	Gly	Ser	Gly	Glu	130	135	140
Leu	Thr	Thr	Gln	Ile	Pro	Cys	Ser	Trp	Arg	Thr	Lys	Gly	His	Ile	His	145	150	155
Asp	Lys	Lys	Thr	Glu	Pro	Phe	Arg	Leu	Leu	Ala	Trp	Ser	Trp	Cys	Leu	165	170	175
Asn	Asp	Glu	Gln	Phe	Leu	Gly	Phe	Gly	Ser	Asp	Glu	Glu	Val	Arg	Val	180	185	190
Arg	Ser	Pro	Thr	Arg	Ser	Pro	Ser	Val	Lys	Thr	Ser	Pro	Arg	Lys	Pro	195	200	205
Arg	Gly	Arg	Pro	Arg	Ser	Gly	Ser	Asp	Arg	Asn	Ser	Ala	Ile	Leu	Ser	210	215	220
Asp	Pro	Ser	Val	Phe	Ser	Pro	Leu	Asn	Lys	Ser	Glu	Thr	Lys	Ser	Gly	225	230	235
Asp	Lys	Ile	Lys	Lys	Lys	Asp	Ser	Lys	Ser	Ile	Glu	Lys	Lys	Arg	Gly	245	250	255
Arg	Pro	Pro	Thr	Phe	Pro	Gly	Val	Lys	Ile	Lys	Ile	Thr	His	Gly	Lys	260	265	270
Asp	Ile	Ser	Glu	Leu	Pro	Lys	Gly	Asn	Lys	Glu	Asp	Ser	Leu	Lys	Lys	275	280	285
Ile	Lys	Arg	Thr	Pro	Ser	Ala	Thr	Phe	Gln	Gln	Ala	Thr	Lys	Ile	Lys	290	295	300
Lys	Leu	Arg	Ala	Gly	Lys	Leu	Ser	Pro	Leu	Lys	Ser	Lys	Phe	Lys	Thr	305	310	315
Gly	Lys	Leu	Gln	Ile	Gly	Arg	Lys	Gly	Val	Gln	Ile	Val	Arg	Arg	Arg	325	330	335
Gly	Arg	Pro	Pro	Ser	Thr	Glu	Arg	Ile	Lys	Thr	Pro	Ser	Gly	Leu	Leu	340	345	350
Ile	Asn	Ser	Glu	Leu	Glu	Lys	Pro	Gln	Lys	Val	Arg	Lys	Asp	Lys	Glu	355	360	365
Gly	Thr	Pro	Pro	Leu	Thr	Lys	Glu	Asp	Lys	Thr	Val	Val	Arg	Gln	Ser	370	375	380
Pro	Arg	Arg	Ile	Lys	Pro	Val	Arg	Ile	Ile	Pro	Ser	Ser	Lys	Arg	Thr	385	390	395
Asp	Ala	Thr	Ile	Ala	Lys	Gln	Leu	Leu	Gln	Arg	Ala	Lys	Lys	Gly	Ala	405	410	415

38/299

Gln Lys Lys Ile Glu Lys Glu Ala Ala Gln Leu Gln Gly Arg Lys Val  
 420 425 430  
 Lys Thr Gln Val Lys Asn Ile Arg Gln Phe Ile Met Pro Val Val Ser  
 435 440 445  
 Ala Ile Ser Ser Arg Ile Ile Lys Thr Pro Arg Arg Phe Ile Glu Asp  
 450 455 460  
 Glu Asp Tyr Asp Pro Pro Ile Lys Ile Ala Arg Leu Glu Ser Thr Pro  
 465 470 475 480  
 Asn Ser Arg Phe Ser Ala Pro Ser Cys Gly Ser Ser Glu Lys Ser Ser  
 485 490 495  
 Ala Ala Ser Gln His Ser Ser Gln Met Ser Ser Asp Ser Ser Arg Ser  
 500 505 510  
 Ser Ser Pro Ser Val Asp Thr Ser Thr Asp Ser Gln Ala Ser Glu Glu  
 515 520 525  
 Ile Gln Val Leu Pro Glu Glu Arg Ser Asp Thr Pro Glu Val His Pro  
 530 535 540  
 Pro Leu Pro Ile Ser Gln Ser Pro Glu Asn Glu Ser Asn Asp Arg Arg  
 545 550 555 560  
 Ser Arg Arg Tyr Ser Val Ser Glu Arg Ser Phe Gly Ser Arg Thr Thr  
 565 570 575  
 Lys Lys Leu Ser Thr Leu Gln Ser Ala Pro Gln Gln Gln Thr Ser Ser  
 580 585 590  
 Ser Pro Pro Pro Pro Leu Leu Thr Pro Pro Pro Pro Leu Gln Pro Ala  
 595 600 605  
 Ser Ser Ile Ser Asp His Thr Pro Trp Leu Met Pro Pro Thr Ile Pro  
 610 615 620  
 Phe Gly Leu Cys Ser Asn Asn Pro Leu Thr Ser Pro Phe Leu Pro Ala  
 625 630 635 640  
 Ser Thr Ala Pro Met Gln Gly Lys Arg Lys Ser Ile Leu Arg Glu Pro  
 645 650 655  
 Thr Phe Arg Trp Thr Ser Leu Lys His Ser Arg Ser Glu Pro Gln Tyr  
 660 665 670  
 Phe Ser Ser Ala Lys Tyr Ala Lys Glu Gly Leu Ile Arg Lys Pro Ile  
 675 680 685  
 Phe Asp Asn Phe Arg Pro Pro Pro Leu Thr Pro Glu Asp Val Gly Phe  
 690 695 700  
 Ala Ser Gly Phe Ser Ala Ser Gly Thr Ala Ala Ser Ala Arg Leu Phe  
 705 710 715 720  
 Ser Pro Leu His Ser Gly Thr Arg Phe Asp Met His Lys Arg Ser Pro

39/299

725										730					735				
Leu	Leu	Arg	Ala	Pro	Arg	Phe	Thr	Pro	Ser	Glu	Ala	His	Ser	Arg	Ile				
			740												750				
Phe	Glu	Ser	Val	Thr	Leu	Pro	Ser	Asn	Arg	Thr	Ser	Ala	Gly	Thr	Ser				
			755												765				
Ser	Ser	Gly	Val	Ser	Asn	Arg	Lys	Arg	Lys	Arg	Lys	Val	Phe	Ser	Pro				
			770												780				
Ile	Arg	Ser	Glu	Pro	Arg	Ser	Pro	Ser	His	Ser	Met	Arg	Thr	Arg	Ser				
															800				
Gly	Arg	Leu	Ser	Ser	Ser	Glu	Leu	Ser	Pro	Leu	Thr	Pro	Pro	Ser	Ser				
															815				
Val	Ser	Ser	Ser	Leu	Ser	Ile	Ser	Val	Ser	Pro	Leu	Ala	Thr	Ser	Ala				
															830				
Leu	Asn	Pro	Thr	Phe	Thr	Phe	Pro	Ser	His	Ser	Leu	Thr	Gln	Ser	Gly				
															845				
Glu	Ser	Ala	Glu	Lys	Asn	Gln	Arg	Pro	Arg	Lys	Gln	Thr	Ser	Ala	Pro				
															860				
Ala	Glu	Pro	Phe	Ser	Ser	Ser	Ser	Pro	Thr	Pro	Leu	Phe	Pro	Trp	Phe				
															880				
Thr	Pro	Gly	Ser	Gln	Thr	Glu	Arg	Gly	Arg	Asn	Lys	Asp	Lys	Ala	Pro				
															895				
Glu	Glu	Leu	Ser	Lys	Asp	Arg	Asp	Ala	Asp	Lys	Ser	Val	Glu	Lys	Asp				
															910				
Lys	Ser	Arg	Glu	Arg	Asp	Arg	Glu	Arg	Glu	Lys	Glu	Asn	Lys	Arg	Glu				
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Ser	Arg	Lys	Glu	Lys	Arg	Lys	Lys	Gly	Ser	Glu	Ile	Gln	Ser	Ser	Ser				
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Ala	Leu	Tyr	Pro	Val	Gly	Arg	Val	Ser	Lys	Glu	Lys	Val	Val	Gly	Glu				
															960				
Asp	Val	Ala	Thr	Ser	Ser	Ser	Ala	Lys	Lys	Ala	Thr	Gly	Arg	Lys	Lys				
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Ser	Ser	Ser	His	Asp	Ser	Gly	Thr	Asp	Ile	Thr	Ser	Val	Thr	Leu	Gly				
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Asp	Thr	Thr	Ala	Val	Lys	Thr	Lys	Ile	Leu	Ile	Lys	Lys	Gly	Arg	Gly				
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Asn	Leu	Glu	Lys	Thr	Asn	Leu	Asp	Leu	Gly	Pro	Thr	Ala	Pro	Ser	Leu				
															1020				
Glu	Lys	Glu	Lys	Thr	Leu	Cys	Leu	Ser	Thr	Pro	Ser	Ser	Ser	Thr	Val				
															1040				

40/299

Lys His Ser Thr Ser Ser Ile Gly Ser Met Leu Ala Gln Ala Asp Lys  
 1045 1050 1055

Leu Pro Met Thr Asp Lys Arg Val Ala Ser Leu Leu Lys Lys Ala Lys  
 1060 1065 1070

Ala Gln Leu Cys Lys Ile Glu Lys Ser Lys Ser Leu Lys Gln Thr Asp  
 1075 1080 1085

Gln Pro Lys Ala Gln Gly Gln Glu Ser Asp Ser Ser Glu Thr Ser Val  
 1090 1095 1100

Arg Gly Pro Arg Ile Lys His Val Cys Arg Arg Ala Ala Val Ala Leu  
 1105 1110 1115 1120

Gly Arg Lys Arg Ala Val Phe Pro Asp Asp Met Pro Thr Leu Ser Ala  
 1125 1130 1135

Leu Pro Trp Glu Glu Arg Glu Lys Ile Leu Phe Ser Met Gly Asn Asp  
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Asp Lys Ser Ser Ile Ala Gly Ser Glu Asp Ala Glu Pro Leu Ala Pro  
 1155 1160 1165

Pro Ile Lys Pro Ile Lys Pro Val Thr Arg Asn Lys Ala Pro Gln Glu  
 1170 1175 1180

Pro Pro Val Lys Lys Gly Arg Arg Ser Arg Arg Cys Gly Gln Cys Pro  
 1185 1190 1195 1200

Gly Cys Gln Val Pro Glu Asp Cys Gly Val Cys Thr Asn Cys Leu Asp  
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Lys Pro Lys Phe Gly Gly Arg Asn Ile Lys Lys Gln Cys Cys Lys Met  
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Arg Lys Cys Gln Asn Leu Gln Trp Met Pro Ser Lys Ala Tyr Leu Gln  
 1235 1240 1245

Lys Gln Ala Lys Ala Val Lys Lys Lys Glu Lys Lys Ser Lys Thr Ser  
 1250 1255 1260

Glu Lys Lys Asp Ser Lys Glu Ser Ser Val Val Lys Asn Val Val Asp  
 1265 1270 1275 1280

Ser Ser Gln Lys Pro Thr Pro Ser Ala Arg Glu Asp Pro Ala Pro Lys  
 1285 1290 1295

Lys Ser Ser Ser Glu Pro Pro Pro Arg Lys Pro Val Glu Glu Lys Ser  
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Glu Glu Gly Asn Val Ser Ala Pro Gly Pro Glu Ser Lys Gln Ala Thr  
 1315 1320 1325

Thr Pro Ala Ser Arg Lys Ser Ser Lys Gln Val Ser Gln Pro Ala Leu  
 1330 1335 1340

41/299

Val Ile Pro Pro Gln Pro Pro Thr Thr Gly Pro Pro Arg Lys Glu Val  
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 Glu Ser Gly Pro Glu Gln Ser Lys Gln Lys Lys Val Ala Pro Arg Pro  
 1380 1385 1390  
 Ser Ile Pro Val Lys Gln Lys Pro Lys Glu Lys Glu Lys Pro Pro Pro  
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 Ser Asn Gly Asn Ser Ser Lys Gln Lys Ile Pro Ala Asp Gly Val His  
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 1460 1465 1470  
 Thr Ala Ile His Thr Pro Ser Thr Ala Glu Pro Ser Lys Phe Pro Phe  
 1475 1480 1485  
 Pro Thr Lys Asp Ser Gln His Val Ser Ser Val Thr Gln Asn Gln Lys  
 1490 1495 1500  
 Gln Tyr Asp Thr Ser Ser Lys Thr His Ser Asn Ser Gln Gln Gly Thr  
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 Ser Ser Met Leu Glu Asp Asp Leu Gln Leu Ser Asp Ser Glu Asp Ser  
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 Asp Ser Glu Gln Thr Pro Glu Lys Pro Pro Ser Ser Ser Ala Pro Pro  
 1540 1545 1550  
 Ser Ala Pro Gln Ser Leu Pro Glu Pro Val Ala Ser Ala His Ser Ser  
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 1620 1625 1630  
 Pro Gly Ala Gln Ser Pro His Gly Gly Thr Gln Arg Val Arg Ala Ala  
 1635 1640 1645  
 Ala Thr Val Pro Arg Val Arg Ser Ile Leu Asn Pro Lys Ile Leu Pro



42/299

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Leu Lys Ala Pro Ala Lys Pro Pro Arg Pro Pro Glu Ala Pro His Pro		
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Gly Lys Arg Ser Cys Gln Lys Ser Pro Ala Gln Gln Glu Pro Pro Gln		
	1685	1690 1695
Arg Gln Thr Val Gly Thr Lys Gln Pro Lys Lys Pro Val Lys Ala Ser		
	1700	1705 1710
Ala Arg Ala Gly Ser Arg Thr Ser Leu Gln Gly Glu Arg Glu Pro Gly		
	1715	1720 1725
Leu Leu Pro Tyr Gly Ser Arg Asp Gln Thr Ser Lys Asp Lys Pro Lys		
	1730	1735 1740
Val Lys Thr Lys Gly Arg Pro Arg Ala Ala Ala Ser Asn Glu Pro Lys		
	1745	1750 1755 1760
Pro Ala Val Pro Pro Ser Ser Glu Lys Lys Lys His Lys Ser Ser Leu		
	1765	1770 1775
Pro Ala Pro Ser Lys Ala Leu Ser Gly Pro Glu Pro Ala Lys Asp Asn		
	1780	1785 1790
Val Glu Asp Arg Thr Pro Glu His Phe Ala Leu Val Pro Leu Thr Glu		
	1795	1800 1805
Ser Gln Gly Pro Pro His Ser Gly Ser Ser Ser Arg Thr Ser Gly Cys		
	1810	1815 1820
Arg Gln Ala Val Val Val Gln Glu Asp Ser Arg Lys Asp Arg Leu Pro		
	1825	1830 1835 1840
Leu Pro Leu Arg Asp Thr Lys Leu Leu Ser Pro Leu Arg Asp Thr Pro		
	1845	1850 1855
Pro Pro Gln Ser Leu Met Val Lys Ile Thr Leu Asp Leu Leu Ser Arg		
	1860	1865 1870
Ile Pro Gln Pro Pro Gly Lys Gly Ser Arg Gln Arg Lys Ala Glu Asp		
	1875	1880 1885
Lys Gln Pro Pro Ala Gly Lys Lys His Ser Ser Glu Lys Arg Ser Ser		
	1890	1895 1900
Asp Ser Ser Ser Lys Leu Ala Lys Lys Arg Lys Gly Glu Ala Glu Arg		
	1905	1910 1915 1920
Asp Cys Asp Asn Lys Lys Ile Arg Leu Glu Lys Glu Ile Lys Ser Gln		
	1925	1930 1935
Ser Ser Ser Ser Ser Ser Ser His Lys Glu Ser Ser Lys Thr Lys Pro		
	1940	1945 1950
Ser Arg Pro Ser Ser Gln Ser Ser Lys Lys Glu Met Leu Pro Pro Pro		
	1955	1960 1965

43/299

Pro Val Ser Ser Ser Ser Gln Lys Pro Ala Lys Pro Ala Leu Lys Arg  
 1970 1975 1980  
 Ser Arg Arg Glu Ala Asp Thr Cys Gly Gln Asp Pro Pro Lys Ser Ala  
 1985 1990 1995 2000  
 Ser Ser Thr Lys Ser Asn His Lys Asp Ser Ser Ile Pro Lys Gln Arg  
 2005 2010 2015  
 Arg Val Glu Gly Lys Gly Ser Arg Ser Ser Ser Glu His Lys Gly Ser  
 2020 2025 2030  
 Ser Gly Asp Thr Ala Asn Pro Phe Pro Val Pro Ser Leu Pro Asn Gly  
 2035 2040 2045  
 Asn Ser Lys Pro Gly Lys Pro Gln Val Lys Phe Asp Lys Gln Gln Ala  
 2050 2055 2060  
 Asp Leu His Met Arg Glu Glu Lys Lys Met Lys Gln Lys Ala Glu Leu  
 2065 2070 2075 2080  
 Met Thr Asp Arg Val Gly Lys Ala Phe Lys Tyr Leu Glu Ala Val Leu  
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 Ser Phe Ile Glu Cys Gly Ile Ala Thr Glu Ser Glu Ser Gln Ser Ser  
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 Lys Ser Ala Tyr Ser Val Tyr Ser Glu Thr Val Asp Leu Ile Lys Phe  
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 2130 2135 2140  
 Lys Ile Phe Ala Val Leu Cys Met Arg Cys Gln Ser Ile Leu Asn Met  
 2145 2150 2155 2160  
 Ala Met Phe Arg Cys Lys Lys Asp Ile Ala Ile Lys Tyr Ser Arg Thr  
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 Pro Cys Ile Ala Arg Ser Thr Gly Thr Pro Ser Pro Leu Ser Pro Met  
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 Asn Met Thr Ser Ser Tyr Val Thr Ile Thr Ser His Val Leu Thr Ala  
 2245 2250 2255  
 Phe Asp Leu Trp Glu Gln Ala Glu Ala Leu Thr Arg Lys Asn Lys Glu  
 2260 2265 2270

44/299

Phe Phe Ala Arg Leu Ser Thr Asn Val Cys Thr Leu Ala Leu Asn Ser  
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Ser Leu Val Asp Leu Val His Tyr Thr Arg Gln Gly Phe Gln Gln Leu  
 2290 2295 2300

Gln Glu Leu Thr Lys Thr Pro  
 2305 2310

&lt;210&gt; 55

&lt;211&gt; 6940

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 55

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46/299

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&lt;210&gt; 56

&lt;211&gt; 277

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 56

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Pro Pro Arg Lys Glu Val Pro Lys Thr Thr Pro Ser Glu Pro Lys Lys
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Lys Gln Pro Pro Pro Pro Glu Ser Gly Pro Glu Gln Ser Lys Gln Lys
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Lys Val Ala Pro Arg Pro Ser Ile Pro Val Lys Gln Lys Pro Lys Glu
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Lys Glu Lys Pro Pro Pro Val Asn Lys Gln Glu Asn Ala Gly Thr Leu
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Asn Ile Phe Ser Thr Leu Ser Asn Gly Asn Ser Ser Lys Gln Lys Ile
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Pro Ala Asp Gly Val His Arg Ile Arg Val Asp Phe Lys Glu Asp Cys
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Glu Ala Glu Asn Val Trp Glu Met Gly Gly Leu Gly Ile Leu Thr Ser
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Val Pro Ile Thr Pro Arg Val Val Cys Phe Leu Cys Ala Ser Ser Gly

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47/299

180	185	190
His Val Glu Thr Tyr Ser Asn Glu Val His Cys Val Glu Glu Ile Leu		
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Lys Glu Met Thr His Ser Trp Pro Pro Pro Leu Thr Ala Ile His Thr		
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Pro Ser Thr Ala Glu Pro Ser Lys Phe Pro Phe Pro Thr Lys Asp Ser		
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Gln His Val Ser Ser Val Thr Gln Asn Gln Lys Gln Tyr Asp Thr Ser		
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49/299

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54/299

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&lt;210&gt; 64

&lt;211&gt; 149

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 64

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Ile His Thr Pro Ser Thr Ala Glu Pro Ser Lys Phe Pro Phe Pro Thr
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```

Lys Asp Ser Gln His Val Ser Ser Val Thr Gln Asn Gln Lys Gln Tyr
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Asp Thr Ser Ser Lys Thr His Ser Asn Ser Gln Gln Gly Thr Ser Ser
    65                      70                      75                      80

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Met Leu Glu Asp Asp Leu Gln Leu Ser Asp Ser Glu Asp Ser Asp Ser
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Glu Gln Thr Pro Glu Lys Pro Pro Ser Ser Ala Pro Pro Ser Ala
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Pro Gln Ser Leu Pro Glu Pro Val Ala Ser Ala His Ser Ser Ser Ala
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Glu Ser Ser Ser Ser
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55/299

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50 55 60  
Asp Thr Ser Ser Lys Thr His Ser Asn Ser Gln Gln Gly Thr Ser Ser  
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Met Leu Glu Asp Asp Leu Gln Leu Ser Asp Ser Glu Asp Ser Asp Ser  
85 90 95  
Glu Gln Thr Pro Glu Lys Pro Pro Ser Ser Ser Ala Pro Pro Ser Ala  
100 105 110  
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56/299

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&lt;210&gt; 68

&lt;211&gt; 6983

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 68

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58/299

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&lt;210&gt; 69

&lt;211&gt; 198

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 69

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Gln Gln Thr Leu Pro Arg Thr Gln Gly Ser Ser Lys Val His Gly Ser
      20              25              30

Ser Asn Asn Ser Lys Gly Tyr Cys Pro Ala Lys Ser Pro Lys Asp Leu
      35              40              45

Ala Val Lys Val His Asp Lys Glu Thr Pro Gln Asp Ser Leu Val Ala
      50              55              60

Pro Ala Gln Pro Pro Ser Gln Thr Phe Pro Pro Pro Ser Leu Pro Ser
      65              70              75              80

Lys Ser Val Ala Met Gln Gln Lys Pro Thr Ala Tyr Val Arg Pro Met
      85              90              95

Asp Gly Gln Asp Gln Ala Pro Ser Glu Ser Pro Glu Leu Lys Pro Leu
      100              105              110

Pro Glu Asp Tyr Arg Gln Gln Thr Phe Glu Lys Thr Asp Leu Lys Val
      115              120              125

Pro Ala Lys Ala Lys Leu Thr Lys Leu Lys Met Pro Ser Gln Ser Val
      130              135              140

Glu Gln Thr Tyr Ser Asn Glu Val His Cys Val Glu Glu Ile Leu Lys
      145              150              155              160

Glu Lys Pro Pro Pro Val Asn Lys Gln Glu Asn Ala Gly Thr Leu Asn
      165              170              175

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59/299

Ile Leu Ser Thr Leu Ser Asn Gly Asn Ser Ser Lys Gln Lys Ile Pro  
 180 185 190

Ala Asp Gly Val His Arg  
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&lt;210&gt; 70

&lt;211&gt; 596

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 70

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&lt;210&gt; 71

&lt;211&gt; 198

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 71

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Ile Ser Leu Pro Ser Pro Val Pro Pro Leu Ser Pro Ile His Ser Asn
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Gln Gln Thr Leu Pro Arg Thr Gln Gly Ser Ser Lys Val His Gly Ser
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Ser Asn Asn Ser Lys Gly Tyr Cys Pro Ala Lys Ser Pro Lys Asp Leu
  35 40 45

Ala Val Lys Val His Asp Lys Glu Thr Pro Gln Asp Ser Leu Val Ala
  50 55 60

Pro Ala Gln Pro Pro Ser Gln Thr Phe Pro Pro Pro Ser Leu Pro Ser
  65 70 75 80

Lys Ser Val Ala Met Gln Gln Lys Pro Thr Ala Tyr Val Arg Pro Met
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Asp Gly Gln Asp Gln Ala Pro Ser Glu Ser Pro Glu Leu Lys Pro Leu
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Pro Glu Asp Tyr Arg Gln Gln Thr Phe Glu Lys Thr Asp Leu Lys Val
  115 120 125

Pro Ala Lys Ala Lys Leu Thr Lys Leu Lys Met Pro Ser Gln Ser Val
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60/299

Glu Gln Thr Tyr Ser Asn Glu Val His Cys Val Glu Glu Ile Leu Lys  
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Glu Lys Pro Pro Pro Val Asn Lys Gln Glu Asn Ala Gly Thr Leu Asn  
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Ile Leu Ser Thr Leu Ser Asn Gly Asn Ser Ser Lys Gln Lys Ile Pro  
 180 185 190

Ala Asp Gly Val His Arg  
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<210> 72  
 <211> 596  
 <212> DNA  
 <213> Homo sapiens

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 ccagccaaat ctccaagga cctagcagtg aaagtccatg ataaagagac ccctcaagac 180  
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 <212> DNA  
 <213> Homo sapiens

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<210> 74  
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 <212> DNA  
 <213> Homo sapiens

61/299

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&lt;210&gt; 75

&lt;211&gt; 60

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 75

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&lt;210&gt; 76

&lt;211&gt; 74

62/299

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 76

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&lt;210&gt; 77

&lt;211&gt; 84

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 77

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&lt;210&gt; 78

&lt;211&gt; 501

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 78

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Arg Pro Glu Ile Ala Asn Gln Pro Ser Glu Pro Pro Glu Val Glu Pro  
35 40 45  
Asp Leu Gly Glu Lys Val His Thr Glu Gly Arg Ser Glu Pro Ile Leu  
50 55 60  
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145 150 155 160  
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165 170 175  
Asn Pro Glu Gly Gly Lys Ser Gly Lys Ala Pro Arg Arg Arg Ala Ala

63/299

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Ser	Ser	Asn	Ala	Ser	Ser	Val	Ser	Thr	Arg	Leu	Ser	Pro	Leu	Arg	Pro
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Glu	Ser	Glu	Val	Leu	Ala	Glu	Glu	Ile	Pro	Ala	Ser	Val	Ser	Ser	Tyr
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Glu	Gly	Cys	Phe	Ser	Ser	Ser	Gln	Ala	Leu	Glu	Ala	Leu	Leu	Thr	Ser
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Asp	Leu	Asp	Leu	Asp	Met	Tyr	Met	Glu	Asn	Leu	Glu	Cys	Asp	Met	Asp
465					470					475					480
Asn	Ile	Ile	Ser	Asp	Leu	Met	Asp	Glu	Gly	Glu	Gly	Leu	Asp	Phe	Asn
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Phe Glu Pro Asp Pro  
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<210> 79

<211> 3171

<212> DNA

<213> Homo sapiens

<400> 79

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atatctactc	tttacccttg	agccctcccc	aggaatttgg	gacctgtctt	tagagctagg	1800
gtggggctct	gtcacacaca	gggtgttgaag	aaattataaa	gataaagctg	ccccatctgg	1860
ggacgatatg	gggagggaga	tgggagggga	aaggggagag	ggtttttctc	actgtgccaa	1920
ttagggggta	aggccccctc	tcaggagcca	tcatcggtct	tccccattcc	taccacttta	1980
ggctttgtag	caagatgagc	aatgctgttg	gaaatgtgaa	gtcaccagtg	gccttacccc	2040
tgcctttggg	agcaggattt	ttttgtagag	agtcttatct	gagctgagcc	aggctagctg	2100
gagcctggga	tttctatgca	gtggccccct	aggccagtga	tgtgcgggtg	gtgggctgtt	2160
taggggatct	ggaagggcca	aggtctgagc	actggagtg	ctcgccaggc	caaatcacc	2220
ttagaaggct	gcagataaca	gaaaggcttt	ttataaaact	ttaaagaaat	ataaacacaa	2280
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acagggaggt	ggggagaggt	ggggagtaat	agtaaacaca	gggaagagct	cccctacgga	2460
ccaggtatag	agaaaggctc	atgcagaaat	aggttagagt	ttccctaaca	aaaaagctaa	2520
cccagggtccc	ctcattccct	caacttgtgc	ctgggagtg	gtgggtgttag	gggtgcagcca	2580
cactcttcta	tgaccagcca	tgggttagtg	ctatggtggg	agagtacatt	gaaggcctgg	2640
aattagcttg	gggcccaggga	agggactggg	aggggagaga	agagaaggag	ggaaggattt	2700
aggatggtaa	agttagggtac	agagacctcc	ctgttcaagg	cccctgacag	ctgtccctgc	2760
ccttcttccc	cttccctgac	tgcagggggt	atgtggaagt	gtgtgtggca	gcaggcagcg	2820

65/299

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gggagggggag gaacaggggaa ggggggagctg gggagcttgg ctgaggggtct gggaaatgag 2880
cagggatggg gggggatgtg gatcagggtt actagcacct gccagggagg ccatctgggg 2940
ctccttctcc accccagccc ccaaagcagc ccttccccca gtgccctttg catcgtcccc 3000
tccccacccc ctgctgtggg ttcccatcat ttcctgtgtc agcgctggc ctaccagat 3060
tgtatcatgt gctagattgg agtggggaag tgtgtcaaat caataaatga ataaattcaa 3120
taaatgccta taaccagcag aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa a 3171

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&lt;210&gt; 80

&lt;211&gt; 501

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 80

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Met Arg Ile Gln Pro Gln Lys Ala Ala Ala Ile Ile Asp Leu Asp Pro
  1                               10                      15

Asp Phe Glu Pro Gln Ser Arg Pro Arg Ser Cys Thr Trp Pro Leu Pro
          20                      25                      30

Arg Pro Glu Ile Ala Asn Gln Pro Ser Glu Pro Pro Glu Val Glu Pro
          35                      40                      45

Asp Leu Gly Glu Lys Val His Thr Glu Gly Arg Ser Glu Pro Ile Leu
          50                      55                      60

Leu Pro Ser Arg Leu Ser Glu Pro Ala Gly Gly Pro Gln Pro Gly Ile
          65                      70                      75                      80

Leu Gly Ala Val Thr Gly Pro Arg Lys Gly Gly Ser Arg Arg Asn Ala
          85                      90                      95

Trp Gly Asn Gln Ser Tyr Ala Glu Phe Ile Ser Gln Ala Ile Glu Ser
          100                      105                      110

Ala Pro Glu Lys Arg Leu Thr Leu Ala Gln Ile Tyr Glu Trp Met Val
          115                      120                      125

Arg Thr Val Pro Tyr Phe Lys Asp Lys Gly Asp Ser Asn Ser Ser Ala
          130                      135                      140

Gly Trp Lys Asn Ser Ile Arg His Asn Leu Ser Leu His Ser Lys Phe
          145                      150                      155                      160

Ile Lys Val His Asn Glu Ala Thr Gly Lys Ser Ser Trp Trp Met Leu
          165                      170                      175

Asn Pro Glu Gly Gly Lys Ser Gly Lys Ala Pro Arg Arg Arg Ala Ala
          180                      185                      190

Ser Met Asp Ser Ser Ser Lys Leu Leu Arg Gly Arg Ser Lys Ala Pro
          195                      200                      205

Lys Lys Lys Pro Ser Val Leu Pro Ala Pro Pro Glu Gly Ala Thr Pro
          210                      215                      220

Thr Ser Pro Val Gly His Phe Ala Lys Trp Ser Gly Ser Pro Cys Ser
          225                      230                      235                      240

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66/299

Arg Asn Arg Glu Glu Ala Asp Met Trp Thr Thr Phe Arg Pro Arg Ser  
 245 250 255  
 Ser Ser Asn Ala Ser Ser Val Ser Thr Arg Leu Ser Pro Leu Arg Pro  
 260 265 270  
 Glu Ser Glu Val Leu Ala Glu Glu Ile Pro Ala Ser Val Ser Ser Tyr  
 275 280 285  
 Ala Gly Gly Val Pro Pro Thr Leu Asn Glu Gly Leu Glu Leu Leu Asp  
 290 295 300  
 Gly Leu Asn Leu Thr Ser Ser His Ser Leu Leu Ser Arg Ser Gly Leu  
 305 310 315 320  
 Ser Gly Phe Ser Leu Gln His Pro Gly Val Thr Gly Pro Leu His Thr  
 325 330 335  
 Tyr Ser Ser Ser Leu Phe Ser Pro Ala Glu Gly Pro Leu Ser Ala Gly  
 340 345 350  
 Glu Gly Cys Phe Ser Ser Ser Gln Ala Leu Glu Ala Leu Leu Thr Ser  
 355 360 365  
 Asp Thr Pro Pro Pro Pro Ala Asp Val Leu Met Thr Gln Val Asp Pro  
 370 375 380  
 Ile Leu Ser Gln Ala Pro Thr Leu Leu Leu Leu Gly Gly Leu Pro Ser  
 385 390 395 400  
 Ser Ser Lys Leu Ala Thr Gly Val Gly Leu Cys Pro Lys Pro Leu Glu  
 405 410 415  
 Ala Arg Gly Pro Ser Ser Leu Val Pro Thr Leu Ser Met Ile Ala Pro  
 420 425 430  
 Pro Pro Val Met Ala Ser Ala Pro Ile Pro Lys Ala Leu Gly Thr Pro  
 435 440 445  
 Val Leu Thr Pro Pro Thr Glu Ala Ala Ser Gln Asp Arg Met Pro Gln  
 450 455 460  
 Asp Leu Asp Leu Asp Met Tyr Met Glu Asn Leu Glu Cys Asp Met Asp  
 465 470 475 480  
 Asn Ile Ile Ser Asp Leu Met Asp Glu Gly Glu Gly Leu Asp Phe Asn  
 485 490 495  
 Phe Glu Pro Asp Pro  
 500

&lt;210&gt; 81

&lt;211&gt; 3171

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

67/299

&lt;400&gt; 81

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gggacagctt agggactatc gtccctgggac taggggggaag ttcgcgactt tctgaagact 60
ggcaggaatg tgcctcctgg ccctcgatgc ttccccctg aggggaggca tcgtagaggga 120
ctgtggcagg cttcactgaa cgctgagccg gggagggtcca actccacgta tggatccggg 180
gaatgagaat tcagccacag aaggccgccc cgatcataga cctagatccc gacttcgaac 240
cccagagccg tccccgctcc tgcacctggc cccttccccg accagagatc gctaaccagc 300
cgtccgagcc gcccagagtg gagccagatc tgggggaaaa ggtacacacg gaggggct 360
cagagccgat cctgttgccc tctcggtctc cagagccggc cgggggcccc cagcccggaa 420
tcctgggggc tgtaacaggt cctcggaagg gaggtccccg ccggaatgcc tggggaaatc 480
agtcatatgc agaattcatc agccaggcca ttgaaagcgc cccggagaag cgactgacac 540
ttgcccagat ttacgagtggt atggtccgta ctgtacccta cttcaaggac aagggtgaca 600
gcaacagctc agcaggatgg aagaactcga tccgccacaa cctgtccctg cacagcaagt 660
tcatcaagggt tcacaacgag gccaccggca aaagctcttg gtggatgctg aaccctgagg 720
gaggcaagag cggcaaagcc ccccgccgcc gggccgcctc catggatagc agcagcaagc 780
tgctccgggg ccgcagtaaa gcccccaaga agaaaccatc tgtgctgcca gctccacccg 840
aagggtgccac tccaacgagc cctgtcggcc actttgccaa gtgggtcaggc agcccttgct 900
ctcgaacccg tgaagaagcc gatatgtgga ccaccttccg tccacgaagc agttcaaagt 960
ccagcagtggt cagcaccocg ctgtccccct tgaggccaga gtctgagggt ctggcgagg 1020
aaataccagc ttcagtcagc agttatgcag ggggtgtccc tcccaccctc aatgaagggtc 1080
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acagaatgcc tcaggatcta gatcttgata tgtatatgga gaacctggag tgtgacatgg 1620
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tgtatcatgt gctagattgg agtggggaag tgtgtcaaat caataaatga ataaattcaa 3120
taaattgccta taaccagcag aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa a 3171

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&lt;210&gt; 82

&lt;211&gt; 74

68/299

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 82

ggagtccaca ggatcagagt ggactttaag catgatacca gtagtccttt gctaatacagt 60  
ggaacctctg caga 74

&lt;210&gt; 83

&lt;211&gt; 22

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 83

Lys Gln Pro Pro Pro Glu Ser Gly Phe Gly Val Pro Trp Ser Asp  
1 5 10 15

Glu Ile Leu Phe Ser Arg  
20

&lt;210&gt; 84

&lt;211&gt; 69

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 84

aagcagcctc caccaccaga atcaggattt ggagttccat ggagtgatga gattttattt 60  
tcaagataa 69

&lt;210&gt; 85

&lt;211&gt; 23

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 85

Val Lys Gln Lys Pro Lys Glu Lys Asp Leu Glu Phe His Gly Val Met  
1 5 10 15

Arg Phe Tyr Phe Gln Asp Lys  
20

&lt;210&gt; 86

&lt;211&gt; 69

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 86

gtaaaacaaa aacccaaaaga aaaggatttg gagttccatg gagtgatgag attttatttt 60  
caagataaa 69

&lt;210&gt; 87

&lt;211&gt; 23

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

69/299

&lt;400&gt; 87

His Arg Ile Arg Val Asp Phe Lys Asp Leu Glu Phe His Gly Val Met  
1 5 10 15

Arg Phe Tyr Phe Gln Asp Lys  
20

&lt;210&gt; 88

&lt;211&gt; 69

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 88

cacaggatca gagtggactt taaggatttg gagttccatg gagt gatgag attttatattt 60  
caagataaa 69

&lt;210&gt; 89

&lt;211&gt; 76

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 89

Pro Pro Thr Thr Gly Pro Pro Arg Lys Glu Val Pro Lys Thr Thr Pro  
1 5 10 15

Ser Glu Pro Lys Lys Lys Gln Pro Pro Pro Glu Ser Gly Ile Tyr  
20 25 30

Thr Ser Asn Lys Asp Pro Ile Ser His Ser Gly Gly Met Leu Arg Ala  
35 40 45

Val Cys Ser Thr Pro Leu Ser Ser Ser Leu Leu Gly Pro Pro Gly Thr  
50 55 60

Ser Ala Leu Pro Arg Leu Ser Arg Ser Pro Phe Thr  
65 70 75

&lt;210&gt; 90

&lt;211&gt; 228

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 90

ccacctacta caggaccgcc aagaaaagaa gttcccaaaa ccactcctag tgagcccaag 60  
aaaaagcagc ctccaccacc agaatacaggc atctacacca gtaataagga ccccatctcc 120  
cacagtggcg ggatgctgcg ggctgtctgc agcaccctc tctcctccag cctcctgggg 180  
ccccaggga cctcggcctt gccccgcctc agcgcgtccc cgttcacc 228

&lt;210&gt; 91

&lt;211&gt; 1093

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

70/299

&lt;400&gt; 91

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Met Lys Glu Met Val Gly Gly Cys Cys Val Cys Ser Asp Glu Arg Gly
 1           5           10           15

Trp Ala Glu Asn Pro Leu Val Tyr Cys Asp Gly His Ala Cys Ser Val
          20           25           30

Ala Val His Gln Ala Cys Tyr Gly Ile Val Gln Val Pro Thr Gly Pro
          35           40           45

Trp Phe Cys Arg Lys Cys Glu Ser Gln Glu Arg Ala Ala Arg Val Arg
 50           55           60

Cys Glu Leu Cys Pro His Lys Asp Gly Ala Leu Lys Arg Thr Asp Asn
 65           70           75           80

Gly Gly Trp Ala His Val Val Cys Ala Leu Tyr Ile Pro Glu Val Gln
          85           90           95

Phe Ala Asn Val Leu Thr Met Glu Pro Ile Val Leu Gln Tyr Val Pro
          100          105          110

His Asp Arg Phe Asn Lys Thr Cys Tyr Ile Cys Glu Glu Thr Gly Arg
          115          120          125

Glu Ser Lys Ala Ala Ser Gly Ala Cys Met Thr Cys Asn Arg His Gly
          130          135          140

Cys Arg Gln Ala Phe His Val Thr Cys Ala Gln Met Ala Gly Leu Leu
          145          150          155          160

Cys Glu Glu Glu Val Leu Glu Val Asp Asn Val Lys Tyr Cys Gly Tyr
          165          170          175

Cys Lys Tyr His Phe Ser Lys Met Lys Thr Ser Arg His Ser Ser Gly
          180          185          190

Gly Gly Gly Gly Gly Ala Gly Gly Gly Gly Gly Ser Met Gly Gly Gly
          195          200          205

Gly Ser Gly Phe Ile Ser Gly Arg Arg Ser Arg Ser Ala Ser Pro Ser
          210          215          220

Thr Gln Gln Glu Lys His Pro Thr His His Glu Arg Gly Gln Lys Lys
          225          230          235          240

Ser Arg Lys Asp Lys Glu Arg Leu Lys Gln Lys His Lys Lys Arg Pro
          245          250          255

Glu Ser Pro Pro Ser Ile Leu Thr Pro Pro Val Val Pro Thr Ala Asp
          260          265          270

Lys Val Ser Ser Ser Ala Ser Ser Ser Ser His His Glu Ala Ser Thr
          275          280          285

Gln Glu Thr Ser Glu Ser Ser Arg Glu Ser Lys Gly Lys Lys Ser Ser
          290          295          300

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71/299

Ser His Ser Leu Ser His Lys Gly Lys Lys Leu Ser Ser Gly Lys Gly  
 305 310 315 320  
 Val Ser Ser Phe Thr Ser Ala Ser Ser Ser Ser Ser Ser Ser Ser  
 325 330 335  
 Ser Ser Gly Gly Pro Phe Gln Pro Ala Val Ser Ser Leu Gln Ser Ser  
 340 345 350  
 Pro Asp Phe Ser Ala Phe Pro Lys Leu Glu Gln Pro Glu Glu Asp Lys  
 355 360 365  
 Tyr Ser Lys Pro Thr Ala Pro Ala Pro Ser Ala Pro Pro Ser Pro Ser  
 370 375 380  
 Ala Pro Glu Pro Pro Lys Ala Asp Leu Phe Glu Gln Lys Val Val Phe  
 385 390 395 400  
 Ser Gly Phe Gly Pro Ile Met Arg Phe Ser Thr Thr Thr Ser Ser Ser  
 405 410 415  
 Gly Arg Ala Arg Ala Pro Ser Pro Gly Asp Tyr Lys Ser Pro His Val  
 420 425 430  
 Thr Gly Ser Gly Ala Ser Ala Gly Thr His Lys Arg Met Pro Ala Leu  
 435 440 445  
 Ser Ala Thr Pro Val Pro Ala Asp Glu Thr Pro Glu Thr Gly Leu Lys  
 450 455 460  
 Glu Lys Lys His Lys Ala Ser Lys Arg Ser Arg His Gly Pro Gly Arg  
 465 470 475 480  
 Pro Lys Gly Ser Arg Asn Lys Glu Gly Thr Gly Gly Pro Ala Ala Pro  
 485 490 495  
 Ser Leu Pro Ser Ala Gln Leu Ala Gly Phe Thr Ala Thr Ala Ala Ser  
 500 505 510  
 Pro Phe Ser Gly Gly Ser Leu Val Ser Ser Gly Leu Gly Gly Leu Ser  
 515 520 525  
 Ser Arg Thr Phe Gly Pro Ser Gly Ser Leu Pro Ser Leu Ser Leu Glu  
 530 535 540  
 Ser Pro Leu Leu Gly Ala Gly Ile Tyr Thr Ser Asn Lys Asp Pro Ile  
 545 550 555 560  
 Ser His Ser Gly Gly Met Leu Arg Ala Val Cys Ser Thr Pro Leu Ser  
 565 570 575  
 Ser Ser Leu Leu Gly Pro Pro Gly Thr Ser Ala Leu Pro Arg Leu Ser  
 580 585 590  
 Arg Ser Pro Phe Thr Ser Thr Leu Pro Ser Ser Ser Ala Ser Ile Ser  
 595 600 605  
 Thr Thr Gln Val Phe Ser Leu Ala Gly Ser Thr Phe Ser Leu Pro Ser

72/299

610					615					620					
Thr	His	Ile	Phe	Gly	Thr	Pro	Met	Gly	Ala	Val	Asn	Pro	Leu	Leu	Ser
625					630					635					640
Gln	Ala	Glu	Ser	Ser	His	Thr	Glu	Pro	Asp	Leu	Glu	Asp	Cys	Ser	Phe
				645					650					655	
Arg	Cys	Arg	Gly	Thr	Ser	Pro	Gln	Glu	Ser	Leu	Ser	Ser	Met	Ser	Pro
			660					665					670		
Ile	Ser	Ser	Leu	Pro	Ala	Leu	Phe	Asp	Gln	Thr	Ala	Ser	Ala	Pro	Cys
			675				680					685			
Gly	Gly	Gly	Gln	Leu	Asp	Pro	Ala	Ala	Pro	Gly	Thr	Thr	Asn	Met	Glu
			690			695					700				
Gln	Leu	Leu	Glu	Lys	Gln	Gly	Asp	Gly	Glu	Ala	Gly	Val	Asn	Ile	Val
705						710					715				720
Glu	Met	Leu	Lys	Ala	Leu	His	Ala	Leu	Gln	Lys	Glu	Asn	Gln	Arg	Leu
				725					730					735	
Gln	Glu	Gln	Ile	Leu	Ser	Leu	Thr	Ala	Lys	Lys	Glu	Arg	Leu	Gln	Ile
			740					745					750		
Leu	Asn	Val	Gln	Leu	Ser	Val	Pro	Phe	Pro	Ala	Leu	Pro	Ala	Ala	Leu
			755				760					765			
Pro	Ala	Ala	Asn	Gly	Pro	Val	Pro	Gly	Pro	Tyr	Gly	Leu	Pro	Pro	Gln
			770			775					780				
Ala	Gly	Ser	Ser	Asp	Ser	Leu	Ser	Thr	Ser	Lys	Ser	Pro	Pro	Gly	Lys
785						790					795				800
Ser	Ser	Leu	Gly	Leu	Asp	Asn	Ser	Leu	Ser	Thr	Ser	Ser	Glu	Asp	Pro
				805					810					815	
His	Ser	Gly	Cys	Pro	Ser	Arg	Ser	Ser	Ser	Ser	Leu	Ser	Phe	His	Ser
			820					825					830		
Thr	Pro	Pro	Pro	Leu	Pro	Leu	Leu	Gln	Gln	Ser	Pro	Ala	Thr	Leu	Pro
			835				840					845			
Leu	Ala	Leu	Pro	Gly	Ala	Pro	Ala	Pro	Leu	Pro	Pro	Gln	Pro	Gln	Asn
			850			855					860				
Gly	Leu	Gly	Arg	Ala	Pro	Gly	Ala	Ala	Gly	Leu	Gly	Ala	Met	Pro	Met
865						870					875				880
Ala	Glu	Gly	Leu	Leu	Gly	Gly	Leu	Ala	Gly	Ser	Gly	Gly	Leu	Pro	Leu
				885					890					895	
Asn	Gly	Leu	Leu	Gly	Gly	Leu	Asn	Gly	Ala	Ala	Ala	Pro	Asn	Pro	Ala
			900				905						910		
Ser	Leu	Ser	Gln	Ala	Gly	Gly	Ala	Pro	Thr	Leu	Gln	Leu	Pro	Gly	Cys
			915				920					925			

73/299

Leu Asn Ser Leu Thr Glu Gln Gln Arg His Leu Leu Gln Gln Gln Glu  
 930 935 940  
 Gln Gln Leu Gln Gln Leu Gln Gln Leu Leu Ala Ser Pro Gln Leu Thr  
 945 950 955 960  
 Pro Glu His Gln Thr Val Val Tyr Gln Met Ile Gln Gln Ile Gln Gln  
 965 970 975  
 Lys Arg Glu Leu Gln Arg Leu Gln Met Ala Gly Gly Ser Gln Leu Pro  
 980 985 990  
 Met Ala Ser Leu Leu Ala Gly Ser Ser Thr Pro Leu Leu Ser Ala Gly  
 995 1000 1005  
 Thr Pro Gly Leu Leu Pro Thr Ala Ser Ala Pro Pro Leu Leu Pro Ala  
 1010 1015 1020  
 Gly Ala Leu Val Ala Pro Ser Leu Gly Asn Asn Thr Ser Leu Met Ala  
 1025 1030 1035 1040  
 Ala Ala Ala Ala Ala Ala Ala Val Ala Ala Ala Gly Gly Pro Pro Val  
 1045 1050 1055  
 Leu Thr Ala Gln Thr Asn Pro Phe Leu Ser Leu Ser Gly Ala Glu Gly  
 1060 1065 1070  
 Ser Gly Gly Gly Pro Lys Gly Gly Thr Ala Asp Lys Gly Ala Ser Ala  
 1075 1080 1085  
 Asn Gln Glu Lys Gly  
 1090

&lt;210&gt; 92

&lt;211&gt; 3282

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 92

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atgaaggaga  tggtaggagg  ctgctgcgta  tgttcggacg  agaggggctg  ggccgagAAC  60
ccgctgggtct  actgcatggg  gcacgcgtgc  agcgtggccg  tccaccaagc  ttgctatggc  120
atcggttcagg  tgccaacggg  accctgggttc  tgccggaaat  gtgaatctca  ggagcgagca  180
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agcatcctca  ccccgcccg  ggtccccact  gctgacaagg  tctcctcctc  ggcttctctc  840
tctctccacc  acgagggcag  cagcgaggag  acctctgaga  gcagcagggg  gtcaaagggg  900
aaaaagtctt  ccagccatag  cctgagtcac  aaaggaaga  aactgagcag  tgggaaaggt  960
gtgagcagtt  ttacctccgc  ctctcttct  tctcctcct  ctctcctc  ctctgggggg  1020

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74/299

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ccttctccct cagctcccga gccccccaag gctgaccttt ttgagcagaa ggtgggtcttc 1200
tctggctttg ggcccatcat gcgtttctcc accaccacct ccagctcagg cggggcccg 1260
gcgccctccc ctggggacta taagtctccc cagctcacgg ggtctggggc ctcggcaggc 1320
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&lt;210&gt; 93

&lt;211&gt; 752

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 93

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Met Arg Ile Pro Val Asp Ala Ser Thr Ser Arg Arg Phe Thr Pro Pro
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```

Ser Thr Ala Leu Ser Pro Gly Lys Met Ser Glu Ala Leu Pro Leu Gly
          20             25             30

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Ala Pro Asp Ala Gly Ala Ala Leu Ala Gly Lys Leu Arg Ser Gly Asp
          35             40             45

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```

Arg Ser Met Val Glu Val Leu Ala Asp His Pro Gly Glu Leu Val Arg
          50             55             60

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75/299

Thr	Asp	Ser	Pro	Asn	Phe	Leu	Cys	Ser	Val	Leu	Pro	Thr	His	Trp	Arg	
65					70					75					80	
Cys	Asn	Lys	Thr	Leu	Pro	Ile	Ala	Phe	Lys	Val	Val	Ala	Leu	Gly	Asp	
				85					90					95		
Val	Pro	Asp	Gly	Thr	Leu	Val	Thr	Val	Met	Ala	Gly	Asn	Asp	Glu	Asn	
			100					105					110			
Tyr	Ser	Ala	Glu	Leu	Arg	Asn	Ala	Thr	Ala	Ala	Met	Lys	Asn	Gln	Val	
		115					120					125				
Ala	Arg	Phe	Asn	Asp	Leu	Arg	Phe	Val	Gly	Arg	Ser	Gly	Arg	Gly	Lys	
	130					135					140					
Ser	Phe	Thr	Leu	Thr	Ile	Thr	Val	Phe	Thr	Asn	Pro	Pro	Gln	Val	Ala	
145					150					155					160	
Thr	Tyr	His	Arg	Ala	Ile	Lys	Ile	Thr	Val	Asp	Gly	Pro	Arg	Glu	Pro	
				165					170					175		
Arg	Asn	Arg	Thr	Glu	Lys	His	Ser	Thr	Met	Pro	Asp	Ser	Pro	Val	Asp	
			180						185					190		
Val	Lys	Thr	Gln	Ser	Arg	Leu	Thr	Pro	Pro	Thr	Met	Pro	Pro	Pro	Pro	
		195					200					205				
Thr	Thr	Gln	Gly	Ala	Pro	Arg	Thr	Ser	Ser	Phe	Thr	Pro	Thr	Thr	Leu	
	210					215					220					
Thr	Asn	Gly	Thr	Ser	His	Ser	Pro	Thr	Ala	Leu	Asn	Gly	Ala	Pro	Ser	
225					230					235					240	
Pro	Pro	Asn	Gly	Phe	Ser	Asn	Gly	Pro	Ser	Ser	Ser	Ser	Ser	Ser	Ser	
				245					250					255		
Leu	Ala	Asn	Gln	Gln	Leu	Pro	Pro	Ala	Cys	Gly	Ala	Arg	Gln	Leu	Ser	
		260						265					270			
Lys	Leu	Lys	Arg	Phe	Leu	Thr	Thr	Leu	Gln	Gln	Phe	Gly	Asn	Asp	Ile	
		275					280					285				
Ser	Pro	Glu	Ile	Gly	Glu	Arg	Val	Arg	Thr	Leu	Val	Leu	Gly	Leu	Val	
	290					295					300					
Asn	Ser	Thr	Leu	Thr	Ile	Glu	Glu	Phe	His	Ser	Lys	Leu	Gln	Glu	Ala	
305					310					315					320	
Thr	Asn	Phe	Pro	Leu	Arg	Pro	Phe	Val	Ile	Pro	Phe	Leu	Lys	Ala	Asn	
				325					330					335		
Leu	Pro	Leu	Leu	Gln	Arg	Glu	Leu	Leu	His	Cys	Ala	Arg	Leu	Ala	Lys	
			340					345					350			
Gln	Asn	Pro	Ala	Gln	Tyr	Leu	Ala	Gln	His	Glu	Gln	Leu	Leu	Leu	Asp	
		355					360					365				
Ala	Ser	Thr	Thr	Ser	Pro	Val	Asp	Ser	Ser	Glu	Leu	Leu	Leu	Asp	Val	

76/299

370		375		380
Asn Glu Asn Gly Lys Arg Arg Thr Pro Asp Arg Thr Lys Glu Asn Gly				
385		390		395
Phe Asp Arg Glu Pro Leu His Ser Glu His Pro Ser Lys Arg Pro Cys				
	405		410	415
Thr Ile Ser Pro Gly Gln Arg Tyr Ser Pro Asn Asn Gly Leu Ser Tyr				
	420		425	430
Gln Pro Asn Gly Leu Pro His Pro Thr Pro Pro Pro Pro Gln His Tyr				
	435		440	445
Arg Leu Asp Asp Met Ala Ile Ala His His Tyr Arg Asp Ser Tyr Arg				
	450		455	460
His Pro Ser His Arg Asp Leu Arg Asp Arg Asn Arg Pro Met Gly Leu				
	465		470	475
His Gly Thr Arg Gln Glu Glu Met Ile Asp His Arg Leu Thr Asp Arg				
	485		490	495
Glu Trp Ala Glu Glu Trp Lys His Leu Asp His Leu Leu Asn Cys Ile				
	500		505	510
Met Asp Met Val Glu Lys Thr Arg Arg Ser Leu Thr Val Leu Arg Arg				
	515		520	525
Cys Gln Glu Ala Asp Arg Glu Glu Leu Asn Tyr Trp Ile Arg Arg Tyr				
	530		535	540
Ser Asp Ala Glu Asp Leu Lys Lys Gly Gly Gly Ser Ser Ser Ser His				
	545		550	555
Ser Arg Gln Gln Ser Pro Val Asn Pro Asp Pro Val Ala Leu Asp Ala				
	565		570	575
His Arg Glu Phe Leu His Arg Pro Ala Ser Gly Tyr Val Pro Glu Glu				
	580		585	590
Ile Trp Lys Lys Ala Glu Glu Ala Val Asn Glu Val Lys Arg Gln Ala				
	595		600	605
Met Thr Glu Leu Gln Lys Ala Val Ser Glu Ala Glu Arg Lys Ala His				
	610		615	620
Asp Met Ile Thr Thr Glu Arg Ala Lys Met Glu Arg Thr Val Ala Glu				
	625		630	635
Ala Lys Arg Gln Ala Ala Glu Asp Ala Leu Ala Val Ile Asn Gln Gln				
	645		650	655
Glu Asp Ser Ser Glu Ser Cys Trp Asn Cys Gly Arg Lys Ala Ser Glu				
	660		665	670
Thr Cys Ser Gly Cys Asn Thr Ala Arg Tyr Cys Gly Ser Phe Cys Gln				
	675		680	685

77/299

His Lys Asp Trp Glu Lys His His His Ile Cys Gly Gln Thr Leu Gln  
 690 695 700

Ala Gln Gln Gln Gly Asp Thr Pro Ala Val Ser Ser Ser Val Thr Pro  
 705 710 715 720

Asn Ser Gly Ala Gly Ser Pro Met Asp Thr Pro Pro Ala Ala Thr Pro  
 725 730 735

Arg Ser Thr Thr Pro Gly Thr Pro Ser Thr Ile Glu Thr Thr Pro Arg  
 740 745 750

&lt;210&gt; 94

&lt;211&gt; 4272

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 94

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 acgctgcccc gccctgcgcc gccaggcact tctttccggg gctcctaggg acgccagaag 120  
 gaagtcaacc tctgctgctt ctcttggcc tgcgttgac cttccttttt ttgttgtttt 180  
 tttttgtttt tcccccttct tccttttgaa ttaactggct tcttggtgg atgttttcaa 240  
 cttctttcct ggctgcgaac ttttcccaa ttgttttcct tttacaacag ggggagaaaag 300  
 tgctctgtgg tccgaggcga gccgtgaagt tgcgtgtgcg tggcagtgtg cgtggcagga 360  
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 gcagctaacc ggcggtgct gggcgacggg ggaggagtat cgtctcgctg ctgcccagat 540  
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 cgactgggccc ttcttatgat tgttgtttta agattagctg aagatctctg aaacgctgaa 780  
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 cagcgtacat taatggattt ctgttgtgtt taaattctcc acagattgta ttgtaaatat 960  
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 gccttgttac gggagataat tgtgttctgt tgggacttta gacaaaactc acctgcaaaa 1140  
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 ctgcctacgc actggcgctg caacaagacc ctgccatcg ctttcaaggt ggtggcccta 1860  
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 aaccaccgc aagtcgccac ctaccacaga gccatcaaaa tcacagtga tgggccccga 2100  
 gaacctcgaa atcgtactga gaagcactcc acaatgccag actcacctgt ggatgtgaag 2160  
 acgcaatcta ggctgactcc tccaacaatg ccacctcccc caactactca aggagctcca 2220  
 agaaccagtt catttacacc gacaacgtta actaatggca cgagccattc tcctacagcc 2280

78/299

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atacaataat gg 4272

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&lt;210&gt; 95

&lt;211&gt; 588

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 95

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Ala Ile Lys Ile Thr Val Asp Gly Pro Arg Glu Pro Arg Asn Arg Thr
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Glu Lys His Ser Thr Met Pro Asp Ser Pro Val Asp Val Lys Thr Gln
      20                               25                      30

Ser Arg Leu Thr Pro Pro Thr Met Pro Pro Pro Pro Thr Thr Gln Gly
      35                               40                      45

Ala Pro Arg Thr Ser Ser Phe Thr Pro Thr Thr Leu Thr Asn Gly Thr
      50                               55                      60

Ser His Ser Pro Thr Ala Leu Asn Gly Ala Pro Ser Pro Pro Asn Gly
      65                               70                      75                      80

Phe Ser Asn Gly Pro Ser Ser Ser Ser Ser Ser Ser Leu Ala Asn Gln

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79/299

85					90					95					
Gln	Leu	Pro	Pro	Ala	Cys	Gly	Ala	Arg	Gln	Leu	Ser	Lys	Leu	Lys	Arg
			100					105					110		
Phe	Leu	Thr	Thr	Leu	Gln	Gln	Phe	Gly	Asn	Asp	Ile	Ser	Pro	Glu	Ile
		115					120					125			
Gly	Glu	Arg	Val	Arg	Thr	Leu	Val	Leu	Gly	Leu	Val	Asn	Ser	Thr	Leu
	130					135					140				
Thr	Ile	Glu	Glu	Phe	His	Ser	Lys	Leu	Gln	Glu	Ala	Thr	Asn	Phe	Pro
145					150					155					160
Leu	Arg	Pro	Phe	Val	Ile	Pro	Phe	Leu	Lys	Ala	Asn	Leu	Pro	Leu	Leu
				165					170					175	
Gln	Arg	Glu	Leu	Leu	His	Cys	Ala	Arg	Leu	Ala	Lys	Gln	Asn	Pro	Ala
			180					185					190		
Gln	Tyr	Leu	Ala	Gln	His	Glu	Gln	Leu	Leu	Leu	Asp	Ala	Ser	Thr	Thr
	195						200					205			
Ser	Pro	Val	Asp	Ser	Ser	Glu	Leu	Leu	Leu	Asp	Val	Asn	Glu	Asn	Gly
	210					215					220				
Lys	Arg	Arg	Thr	Pro	Asp	Arg	Thr	Lys	Glu	Asn	Gly	Phe	Asp	Arg	Glu
225					230					235					240
Pro	Leu	His	Ser	Glu	His	Pro	Ser	Lys	Arg	Pro	Cys	Thr	Ile	Ser	Pro
				245					250					255	
Gly	Gln	Arg	Tyr	Ser	Pro	Asn	Asn	Gly	Leu	Ser	Tyr	Gln	Pro	Asn	Gly
			260					265					270		
Leu	Pro	His	Pro	Thr	Pro	Pro	Pro	Pro	Gln	His	Tyr	Arg	Leu	Asp	Asp
		275					280					285			
Met	Ala	Ile	Ala	His	His	Tyr	Arg	Asp	Ser	Tyr	Arg	His	Pro	Ser	His
	290					295					300				
Arg	Asp	Leu	Arg	Asp	Arg	Asn	Arg	Pro	Met	Gly	Leu	His	Gly	Thr	Arg
305					310					315					320
Gln	Glu	Glu	Met	Ile	Asp	His	Arg	Leu	Thr	Asp	Arg	Glu	Trp	Ala	Glu
			325						330					335	
Glu	Trp	Lys	His	Leu	Asp	His	Leu	Leu	Asn	Cys	Ile	Met	Asp	Met	Val
			340					345				350			
Glu	Lys	Thr	Arg	Arg	Ser	Leu	Thr	Val	Leu	Arg	Arg	Cys	Gln	Glu	Ala
		355					360					365			
Asp	Arg	Glu	Glu	Leu	Asn	Tyr	Trp	Ile	Arg	Arg	Tyr	Ser	Asp	Ala	Glu
	370					375					380				
Asp	Leu	Lys	Lys	Gly	Gly	Gly	Ser	Ser	Ser	Ser	His	Ser	Arg	Gln	Gln
385					390					395					400

Ser	Pro	Val	Asn	Pro	Asp	Pro	Val	Ala	Leu	Asp	Ala	His	Arg	Glu	Phe
				405					410					415	
Leu	His	Arg	Pro	Ala	Ser	Gly	Tyr	Val	Pro	Glu	Glu	Ile	Trp	Lys	Lys
			420					425					430		
Ala	Glu	Glu	Ala	Val	Asn	Glu	Val	Lys	Arg	Gln	Ala	Met	Thr	Glu	Leu
		435					440					445			
Gln	Lys	Ala	Val	Ser	Glu	Ala	Glu	Arg	Lys	Ala	His	Asp	Met	Ile	Thr
	450					455					460				
Thr	Glu	Arg	Ala	Lys	Met	Glu	Arg	Thr	Val	Ala	Glu	Ala	Lys	Arg	Gln
465					470					475					480
Ala	Ala	Glu	Asp	Ala	Leu	Ala	Val	Ile	Asn	Gln	Gln	Glu	Asp	Ser	Ser
				485					490					495	
Glu	Ser	Cys	Trp	Asn	Cys	Gly	Arg	Lys	Ala	Ser	Glu	Thr	Cys	Ser	Gly
			500					505					510		
Cys	Asn	Thr	Ala	Arg	Tyr	Cys	Gly	Ser	Phe	Cys	Gln	His	Lys	Asp	Trp
		515					520					525			
Glu	Lys	His	His	His	Ile	Cys	Gly	Gln	Thr	Leu	Gln	Ala	Gln	Gln	Gln
	530					535					540				
Gly	Asp	Thr	Pro	Ala	Val	Ser	Ser	Ser	Val	Thr	Pro	Asn	Ser	Gly	Ala
545					550					555					560
Gly	Ser	Pro	Met	Asp	Thr	Pro	Pro	Ala	Ala	Thr	Pro	Arg	Ser	Thr	Thr
				565					570					575	
Pro	Gly	Thr	Pro	Ser	Thr	Ile	Glu	Thr	Thr	Pro	Arg				
			580					585							

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<210> 96
<211> 2217
<212> DNA
<213> Homo sapiens
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<400> 96						
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acaatgccaag	actcacctgt	ggatgtgaag	acgcaatcta	ggctgactcc	tccaacaatg	120
ccacctcccc	caactactca	aggagctcca	agaaccagtt	catttacacc	gacaacgtta	180
actaatggca	cgagccattc	tctctacgcc	ttgaatggcg	ccccctcacc	acccaatggc	240
ttcagcaatg	ggccttcctc	tctctcctcc	tctctctcgg	ctaatcaaca	gctgccccca	300
gcctgtggtg	ccaggcaact	cagcaagctg	aaaaggttcc	ttactacctt	gcgacagttt	360
ggcaatgaca	tttcacccga	gataggagaa	agagttcgca	ccctcgtttc	gggactagt	420
aactccactt	tgacaattga	agaatttcat	tccaaactgc	aagaagctac	taacttccca	480
ctgagacctt	ttgtcatccc	atttttgaag	gccaaacttg	ccctgctgca	gcgtgagctc	540
ctccactgcg	caagactggc	caaacagaa	cctgcccgat	acctcgccca	gcataaacag	600
ctgctttctg	atgccagcac	cacctcacct	gttgactcct	cagagctgct	tctcgatgtg	660
aacgaaaaac	ggaagaggcg	aactccagac	agaaccaaa	aaaatggctt	tgacagagag	720
cccttgcact	cagaacatcc	aagcaagcga	ccatgcacta	ttagccagg	ccagcggtac	780
agtccaaata	acggcttatc	ctaccagccc	aatggcctgc	ctcaccctac	cccacctcca	840

81/299

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cctcagcatt accgttttga tgatatggcc attgcccacc actacagggga ctcctatcga 900
caccccagcc acagggacct cagggacaga aacagacctt tgggggttgca tggcacacgt 960
caagaagaaa tgattgatca cagactaaca gacagagaat gggcagaaga gtggaaacat 1020
cttgaccatc tgtttaaactg cataatggac atggtagaaa aaacaaggcg atctctcacc 1080
gtactaaggc ggtgtcaaga agcagaccgg gaagaattga attactggat cgggcggtac 1140
agtgcgccc aggacttaaa aaaagggtggc ggcagtagca gcagccactc taggcagcag 1200
agtcccgtca acccagaccc agttgcacta gacgcgcacg gggaattcct tcacaggcct 1260
gcgtctggat acgtgccaga ggagatctgg aagaaagctg aggaggccgt caatgagggtg 1320
aagcgccagg cgatgacgga gctgcagaag gccgtgtctg aggcggagcg gaaagcccac 1380
gacatgatca caacagagag ggccaagatg gagcgcacgg tcgccgaggc caaacggcag 1440
gcggcgagg agcactggc agttatcaat cagcaggagg attcaagcga gagttgctgg 1500
aattgtggcc gtaaagcgag tgaaacctgc agtggctgta acacagcccg atactgtggc 1560
tcattttgcc agcacaaga ctgggagaag caccatcaca tctgtggaca gaccctgcag 1620
gccagcagc agggagacac acctgcagtc agtcctctg tcacgcccac cagcggggct 1680
gggagcccga tggacacacc accagcagcc actccgaggt caaccacccc gggaacccct 1740
tccaccatag agacaacccc tcgctagacg tgaactcaga actgtcggag gaaagacaac 1800
acaaccaacg cgaaaccaat tcctcatcct cagatgctca aagttgtttt ttttgtttgt 1860
ttgtttatta gatgaattat cctatttcag tacttcagca agagagaacc taactgtatc 1920
ttgaggtgg agtaaaacac agagggccag taacgggtca taatgactta ttgtggataa 1980
caaagatatc ttttctttag agaactgaaa agagagcaga gaatataaca tgaaatgata 2040
gatttgacct cctccctgaa attttcaagt agctgggatt ttaaactaga tgacctcatt 2100
aaccgatgct ttaccaaca ccaaaccaag agattgctaa ttgctgttga aagcaaaaat 2160
gctaataatta aaagtcacaa tgttctttat atacaataat ggaaaaaaaa aaaaaaa 2217

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&lt;210&gt; 97

&lt;211&gt; 231

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 97

```

Ala Ile Lys Ile Thr Val Asp Gly Pro Arg Glu Pro Arg Asn Arg Thr
  1                      5                      10                     15

Glu Lys His Ser Thr Met Pro Asp Ser Pro Val Asp Val Lys Thr Gln
                      20                      25                     30

Ser Arg Leu Thr Pro Pro Thr Met Pro Pro Pro Pro Thr Thr Gln Gly
                      35                      40                     45

Ala Pro Arg Thr Ser Ser Phe Thr Pro Thr Thr Leu Thr Asn Gly Thr
                      50                      55                     60

Ser His Ser Pro Thr Ala Leu Asn Gly Ala Pro Ser Pro Pro Asn Gly
                      65                      70                     75                     80

Phe Ser Asn Gly Pro Ser Ser Ser Ser Ser Ser Ser Leu Ala Asn Gln
                      85                      90                     95

Gln Leu Pro Pro Ala Cys Gly Ala Arg Gln Leu Ser Lys Leu Lys Arg
                      100                     105                    110

Phe Leu Thr Thr Leu Gln Gln Phe Gly Asn Asp Ile Ser Pro Glu Ile
                      115                     120                    125

Gly Glu Arg Val Arg Thr Leu Val Leu Gly Leu Val Asn Ser Thr Leu
                      130                     135                    140

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82/299

Thr Ile Glu Glu Phe His Ser Lys Leu Gln Glu Ala Thr Asn Phe Pro  
 145 150 155 160

Leu Arg Pro Phe Val Ile Pro Phe Leu Lys Ala Asn Leu Pro Leu Leu  
 165 170 175

Gln Arg Glu Leu Leu His Cys Ala Arg Leu Ala Lys Gln Asn Pro Ala  
 180 185 190

Gln Tyr Leu Ala Gln His Glu Gln Leu Leu Leu Asp Ala Ser Thr Thr  
 195 200 205

Ser Pro Val Asp Ser Ser Glu Leu Leu Leu Asp Val Asn Glu Asn Gly  
 210 215 220

Lys Arg Arg Thr Pro Asp Arg  
 225 230

&lt;210&gt; 98

&lt;211&gt; 1412

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 98

```

gccatcaaaa tcacagtgga tgggccccga gaacctcgaa atcgtactga gaagcactcc 60
acaatgccag actcacctgt ggatgtgaag acgcaatcta ggctgactcc tccaacaatg 120
ccacctcccc caactactca aggagctcca agaaccagtt catttacacc gacaacgtta 180
actaatggca cgagccattc tcctacagcc ttgaatggcg cccctcacc acccaatggc 240
ttcagcaatg ggccttcctc ttcttcctcc tcctctctgg ctaatcaaca gctgccccca 300
gcctgtgggtg ccaggcaact cagcaagctg aaaagggttc ttactaccct gcagcagttt 360
ggcaatgaca tttcaccgga gataggagaa agagtctgca ccctcgttct gggactagt 420
aactccactt tgacaattga agaatttcat tccaaactgc aagaagctac taacttccca 480
ctgagacctt ttgtcatccc atttttgaag gccaaacttg ccctgctgca gcgtgagctc 540
ctccactgcg caagactggc caaacagaa cctgcccagt acctcgcca gcatgaacag 600
ctgcttctgg atgccagcac cacctcacct gttgactcct cagagctgct tctcgatgtg 660
aacgaaaacg ggaagaggcg aactccagac aggtgagagg gaggaggagc ctggatgaac 720
catgaccttt ttcccatacc tgtggcatga ggaaacattt catgtcacia ttaaaccgct 780
ggcctatgtc attcttgcac aatagcaata agccattgtg gccatcttga gaatctggct 840
ctggcctggg attttacaga gttttgaatc tctggcctgg gacagtttgg cttttgtgta 900
ggttaactct ttctgcttgt agtattaaag cgaaatggtg aagacgaatg attttctga 960
tttgccaagt accactgatg gctcttagat gcacatcaat attaaaattc tcattcatta 1020
tgtaatttaa cccaaccaca tattttactt caatatcttg aaattggctg ttcctagttt 1080
ccttaaaatg tgatggtttg gaagcttgct tgtatgtatt tcttaacaca gtacagtagt 1140
tatttgtttt ggttgatat gaactaagag aaaacttctg ggacactaga tgaactgagt 1200
gaagataaga gttatacagt agagacaata gatggtatct ttgctgaaaa ttttacttgt 1260
tagatactgt tctatcagat actgtgctct cataactaag aattctaaga aatgtaaaat 1320
aaaaccactt ctccattaaa ccctacagag taattgttga ataaagcata cacatgaaat 1380
ttcaaaaaaa aaaaaaaaaa aagggcggcc gc 1412

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&lt;210&gt; 99

&lt;211&gt; 198

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 99

Ser Phe Thr Leu Thr Ile Thr Val Phe Thr Asn Pro Pro Gln Val Ala

83/299

1	5	10	15
Thr Tyr His Arg Ala Ile Lys Ile Thr Val Asp Gly Pro Arg Glu Pro	20	25	30
Arg Asn Arg Thr Glu Lys His Ser Thr Met Pro Asp Ser Pro Val Asp	35	40	45
Val Lys Thr Gln Ser Arg Leu Thr Pro Pro Thr Met Pro Pro Pro Pro	50	55	60
Thr Thr Gln Gly Ala Pro Arg Thr Ser Ser Phe Thr Pro Thr Thr Leu	65	70	75
Thr Asn Gly Thr Ser His Ser Pro Thr Ala Leu Asn Gly Ala Pro Ser	85	90	95
Pro Pro Asn Gly Phe Ser Asn Gly Pro Ser Ser Ser Ser Ser Ser Ser	100	105	110
Leu Ala Asn Gln Gln Leu Pro Pro Ala Cys Gly Ala Arg Gln Leu Ser	115	120	125
Lys Leu Lys Arg Phe Leu Thr Thr Leu Gln Gln Phe Gly Asn Asp Ile	130	135	140
Ser Pro Glu Ile Gly Glu Arg Val Arg Thr Leu Val Leu Gly Leu Val	145	150	155
Asn Ser Thr Leu Thr Ile Glu Glu Phe His Ser Lys Leu Gln Glu Ala	165	170	175
Thr Asn Phe Pro Leu Arg Pro Phe Val Ile Pro Phe Leu Lys Val Leu	180	185	190
His Ser Ser Leu Val Val	195		

&lt;210&gt; 100

&lt;211&gt; 799

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 100

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aagcttcaact ctgaccatca ctgtcttcac aaaccacccg caagtcgcca cctaccacag 60
agccatcaaaa atcacagtgg atgggccccg agaacctcga aatcgctactg agaagcactc 120
cacaatgcca gactcacctg tggatgtgaa gacgcaatct aggctgactc ctccaacaat 180
gccacctccc ccaactactc aaggagctcc aagaaccagt tcatttacac cgacaacggt 240
aactaatggc acgagccatt ctctacagc cttgaatggc gccccctcac cacccaatgg 300
cttcagcaat gggccttcct cttcttcctc ctctctctg gctaataaac agctgcccc 360
agcctgtggt gccaggcaac tcagcaagct gaaaagggtt cttactaccc tgcagcagtt 420
tggcaatgac atttcacccg agataggaga aagagttcgc accctcgttc tgggactagt 480
gaactccact ttgacaattg aagaatttca ttccaaactg caagaagcta ctaacttccc 540
actgagacct tttgtcatcc catttttgaa ggtattgcac agttcactgg tcgtgtaaag 600
tattttaaac catattgttg ctaggtcata actgtgtgct tttttagtag atttaggggc 660
tctttgattt aatttaatgg atgaaaacta tctgaatcga ttgtatttat gaccatttcc 720
taagtagtct gaaaattaca aggagtgttt taaataatta cctgaaaaga agtaaagttt 780

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84/299

gaagaagagt ttagaagtc

799

&lt;210&gt; 101

&lt;211&gt; 237

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 101

```

gccccgagaa cctcgaaatc gtactgagaa gcactccaca atgccagact cacctgtgga 60
tgtgaagacg caatctaggc tgactcctcc aacaatgcc cctcccccaa ctactcaagg 120
agctccaaga accagttcat ttacaccgac aacgttaact aatggcacga gccattctcc 180
tacagccttg aatggcgccc cctcaccacc caatggcttc agcaatgggc cttcctc 237

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&lt;210&gt; 102

&lt;211&gt; 276

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 102

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gaagtggaag agggaaaagc ttcactctga ccatcactgt cttcaciaaac ccaccgcaag 60
tcgccaccta ccacagagcc atcaaaatca cagtggatgg gccccgagaa cctcgaaata 120
aaccctactt gaaaaactga ggtgcttaag gagtaaaata atatgttcct ggtggcatcc 180
tccagatcgt actgagaagc actccacaat gccagactca cctgtggatg tgaagacgca 240
atctaggctg actcctccaa caatgccacc tcccc 276

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&lt;210&gt; 103

&lt;211&gt; 251

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 103

```

Ser Phe Thr Leu Thr Ile Thr Val Phe Thr Asn Pro Pro Gln Val Ala
 1             5             10             15

Thr Tyr His Arg Ala Ile Lys Ile Thr Val Asp Gly Pro Arg Glu Pro
      20             25             30

Arg Asn Arg Thr Glu Lys His Ser Thr Met Pro Asp Ser Pro Val Asp
      35             40             45

Val Lys Thr Gln Ser Arg Leu Thr Pro Pro Thr Met Pro Pro Pro Pro
 50             55             60

Thr Thr Gln Gly Ala Pro Arg Thr Ser Ser Phe Thr Pro Thr Thr Leu
 65             70             75             80

Thr Asn Gly Thr Ser His Ser Pro Thr Ala Leu Asn Gly Ala Pro Ser
      85             90             95

Pro Pro Asn Gly Phe Ser Asn Gly Pro Ser Ser Ser Ser Ser Ser Ser
      100            105            110

Leu Ala Asn Gln Gln Leu Pro Pro Ala Cys Gly Ala Arg Gln Leu Ser
      115            120            125

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85/299

Lys Leu Lys Arg Phe Leu Thr Thr Leu Gln Gln Phe Gly Asn Asp Ile  
 130 135 140  
 Ser Pro Glu Ile Gly Glu Arg Val Arg Thr Leu Val Leu Gly Leu Val  
 145 150 155 160  
 Asn Ser Thr Leu Thr Ile Glu Glu Phe His Ser Lys Leu Gln Glu Ala  
 165 170 175  
 Thr Asn Phe Pro Leu Arg Pro Phe Val Ile Pro Phe Leu Lys Ala Asn  
 180 185 190  
 Leu Pro Leu Leu Gln Arg Glu Leu Leu His Cys Ala Arg Leu Ala Lys  
 195 200 205  
 Gln Asn Pro Ala Gln Tyr Leu Ala Gln His Glu Gln Leu Leu Leu Asp  
 210 215 220  
 Ala Ser Thr Thr Ser Pro Val Asp Ser Ser Glu Leu Leu Leu Asp Val  
 225 230 235 240  
 Asn Glu Asn Gly Lys Arg Arg Thr Pro Asp Arg  
 245 250

&lt;210&gt; 104

&lt;211&gt; 1446

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 104

```

aagcttcaact ctgaccatca ctgtcttcac aaaccaccg caagtcgcca cctaccacag 60
agccatcaaaa atcacagtgg atgggccccg agaacctcga aatcgtagtg agaagcactc 120
cacaatgccca gactcacctg tggatgtgaa gacgcaatct aggctgactc ctccaacaat 180
gccacctccc ccaactactc aaggagctcc aagaaccagt tcatttacac cgacaacggt 240
aactaatggc acgagccatt ctcttacagc cttgaatggc gccccctcac cacccaatgg 300
cttcagcaat gggccttctt cttcttcctc ctctctcttg gctaataaac agctgcccc 360
agcctgtggg gccaggcaac tcagcaagct gaaaagggtt cttactaccc tgcagcagtt 420
tggcaatgac atttcacccg agataggaga aagagttcgc accctcgttc tgggactagt 480
gaactccact ttgacaattg aagaatttca ttccaaactg caagaagcta ctaacttccc 540
actgagacct tttgtcatcc catttttgaa ggccaacttg cccctgctgc agcgtgagct 600
cctccactgc gcaagactgg ccaaacagaa ccctgcccag tacctcgccc agcatgaaca 660
gctgcttctg gatgccagca ccacctcacc tgttgactcc tcagagctgc ttctcgatgt 720
gaacgaaaac ggggaagagg gaactccaga caggtgagag ggaggaggag cctggatgaa 780
ccatgacctt tttcccatac ctgtggcatg aggaaacatt tcatgtcaca attaaaccgc 840
tggcctatgt cattcttgca caatagcaat aagccattgt ggccatcttg agaatctggc 900
tctggcctgg gattttacag agttttgaat ctctggcctg ggacagtttg gcttttgtgt 960
aggttaattc tttctgcttg tagtattaaa gcgaaatggg gaagacgaat gatttttctg 1020
atttgccaag taccactgat ggctcttaga tgcacatcaa tattaaaatt ctcatcatt 1080
atgtaattta acccaaccac atattttact tcaatattct gaaattggct gttcctagtt 1140
tccttaaaat gtgatggttt ggaagcttgt ctgtatgtat ttcttaacac agtacagtag 1200
ttatttgttt tggttgtata tgaactaaga gaaaacttct gggacactag atgaactgag 1260
tgaagataag agttatacag tagagacaat agatggtatt tttgctgaaa attttacttg 1320
ttagatactg ttctatcaga tactgtgtct tcataactaa gaattctaag aaatgtaaaa 1380
taaaaccact tctccattaa accctacaga gtaattgttg aataaagcat acacatgaaa 1440
tttccc                                     1446

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86/299

&lt;210&gt; 105

&lt;211&gt; 1395

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 105

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Met Arg Ile Pro Val Asp Ala Ser Thr Ser Arg Arg Phe Thr Pro Pro
 1              5              10              15

Ser Thr Ala Leu Ser Pro Gly Lys Met Ser Glu Ala Leu Pro Leu Gly
      20              25              30

Ala Pro Asp Ala Gly Ala Ala Leu Ala Gly Lys Leu Arg Ser Gly Asp
      35              40              45

Arg Ser Met Val Glu Val Leu Ala Asp His Pro Gly Glu Leu Val Arg
      50              55              60

Thr Asp Ser Pro Asn Phe Leu Cys Ser Val Leu Pro Thr His Trp Arg
      65              70              75              80

Cys Asn Lys Thr Leu Pro Ile Ala Phe Lys Val Val Ala Leu Gly Asp
      85              90              95

Val Pro Asp Gly Thr Leu Val Thr Val Met Ala Gly Asn Asp Glu Asn
      100              105              110

Tyr Ser Ala Glu Leu Arg Asn Ala Thr Ala Ala Met Lys Asn Gln Val
      115              120              125

Ala Arg Phe Asn Asp Leu Arg Phe Val Gly Arg Ser Gly Arg Gly Lys
      130              135              140

Ser Phe Thr Leu Thr Ile Thr Val Phe Thr Asn Pro Pro Gln Val Ala
      145              150              155              160

Thr Tyr His Arg Ala Ile Lys Ile Thr Val Asp Gly Pro Arg Glu Pro
      165              170              175

Arg Asn Asn Glu Cys Val Tyr Gly Asn Tyr Pro Glu Ile Pro Leu Glu
      180              185              190

Glu Met Pro Asp Ala Asp Gly Val Ala Ser Thr Pro Ser Leu Asn Ile
      195              200              205

Gln Glu Pro Cys Ser Pro Ala Thr Ser Ser Glu Ala Phe Thr Pro Lys
      210              215              220

Glu Gly Ser Pro Tyr Lys Ala Pro Ile Tyr Ile Pro Asp Asp Ile Pro
      225              230              235              240

Ile Pro Ala Glu Phe Glu Leu Arg Glu Ser Asn Met Pro Gly Ala Gly
      245              250              255

Leu Gly Ile Trp Thr Lys Arg Lys Ile Glu Val Gly Glu Lys Phe Gly
      260              265              270

Pro Tyr Val Gly Glu Gln Arg Ser Asn Leu Lys Asp Pro Ser Tyr Gly

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87/299

275					280					285					
Trp	Glu	Ile	Leu	Asp	Glu	Phe	Tyr	Asn	Val	Lys	Phe	Cys	Ile	Asp	Ala
290						295					300				
Ser	Gln	Pro	Asp	Val	Gly	Ser	Trp	Leu	Lys	Tyr	Ile	Arg	Phe	Ala	Gly
305					310					315					320
Cys	Tyr	Asp	Gln	His	Asn	Leu	Val	Ala	Cys	Gln	Ile	Asn	Asp	Gln	Ile
				325					330					335	
Phe	Tyr	Arg	Val	Val	Ala	Asp	Ile	Ala	Pro	Gly	Glu	Glu	Leu	Leu	Leu
			340					345					350		
Phe	Met	Lys	Ser	Glu	Asp	Tyr	Pro	His	Glu	Thr	Met	Ala	Pro	Asp	Ile
		355					360					365			
His	Glu	Glu	Arg	Gln	Tyr	Arg	Cys	Glu	Asp	Cys	Asp	Gln	Leu	Phe	Glu
	370					375					380				
Ser	Lys	Ala	Glu	Leu	Ala	Asp	His	Gln	Lys	Phe	Pro	Cys	Ser	Thr	Pro
385					390					395					400
His	Ser	Ala	Phe	Ser	Met	Val	Glu	Glu	Asp	Phe	Gln	Gln	Lys	Leu	Glu
				405					410					415	
Ser	Glu	Asn	Asp	Leu	Gln	Glu	Ile	His	Thr	Ile	Gln	Glu	Cys	Lys	Glu
			420					425					430		
Cys	Asp	Gln	Val	Phe	Pro	Asp	Leu	Gln	Ser	Leu	Glu	Lys	His	Met	Leu
	435						440					445			
Ser	His	Thr	Glu	Glu	Arg	Glu	Tyr	Lys	Cys	Asp	Gln	Cys	Pro	Lys	Ala
	450					455					460				
Phe	Asn	Trp	Lys	Ser	Asn	Leu	Ile	Arg	His	Gln	Met	Ser	His	Asp	Ser
465					470					475					480
Gly	Lys	His	Tyr	Glu	Cys	Glu	Asn	Cys	Ala	Lys	Val	Phe	Thr	Asp	Pro
			485						490					495	
Ser	Asn	Leu	Gln	Arg	His	Ile	Arg	Ser	Gln	His	Val	Gly	Ala	Arg	Ala
			500					505					510		
His	Ala	Cys	Pro	Glu	Cys	Gly	Lys	Thr	Phe	Ala	Thr	Ser	Ser	Gly	Leu
	515						520					525			
Lys	Gln	His	Lys	His	Ile	His	Ser	Ser	Val	Lys	Pro	Phe	Ile	Cys	Glu
	530					535					540				
Val	Cys	His	Lys	Ser	Tyr	Thr	Gln	Phe	Ser	Asn	Leu	Cys	Arg	His	Lys
545					550					555					560
Arg	Met	His	Ala	Asp	Cys	Arg	Thr	Gln	Ile	Lys	Cys	Lys	Asp	Cys	Gly
			565					570						575	
Gln	Met	Phe	Ser	Thr	Thr	Ser	Ser	Leu	Asn	Lys	His	Arg	Arg	Phe	Cys
			580					585					590		

88/299

Glu Gly Lys Asn His Phe Ala Ala Gly Gly Phe Phe Gly Gln Gly Ile  
 595 600 605  
 Ser Leu Pro Gly Thr Pro Ala Met Asp Lys Thr Ser Met Val Asn Met  
 610 615 620  
 Ser His Ala Asn Pro Gly Leu Ala Asp Tyr Phe Gly Ala Asn Arg His  
 625 630 635 640  
 Pro Ala Gly Leu Thr Phe Pro Thr Ala Pro Gly Phe Ser Phe Ser Phe  
 645 650 655  
 Pro Gly Leu Phe Pro Ser Gly Leu Tyr His Arg Pro Pro Leu Ile Pro  
 660 665 670  
 Ala Ser Ser Pro Val Lys Gly Leu Ser Ser Thr Glu Gln Thr Asn Lys  
 675 680 685  
 Ser Gln Ser Pro Leu Met Thr His Pro Gln Ile Leu Pro Ala Thr Gln  
 690 695 700  
 Asp Ile Leu Lys Ala Leu Ser Lys His Pro Ser Val Gly Asp Asn Lys  
 705 710 715 720  
 Pro Val Glu Leu Gln Pro Glu Arg Ser Ser Glu Glu Arg Pro Phe Glu  
 725 730 735  
 Lys Ile Ser Asp Gln Ser Glu Ser Ser Asp Leu Asp Asp Val Ser Thr  
 740 745 750  
 Pro Ser Gly Ser Asp Leu Glu Thr Thr Ser Gly Ser Asp Leu Glu Ser  
 755 760 765  
 Asp Ile Glu Ser Asp Lys Glu Lys Phe Lys Glu Asn Gly Lys Met Phe  
 770 775 780  
 Lys Asp Lys Val Ser Pro Leu Gln Asn Leu Ala Ser Ile Asn Asn Lys  
 785 790 795 800  
 Lys Glu Tyr Ser Asn His Ser Ile Phe Ser Pro Ser Leu Glu Glu Gln  
 805 810 815  
 Thr Ala Val Ser Gly Ala Val Asn Asp Ser Ile Lys Ala Ile Ala Ser  
 820 825 830  
 Ile Ala Glu Lys Tyr Phe Gly Ser Thr Gly Leu Val Gly Leu Gln Asp  
 835 840 845  
 Lys Lys Val Gly Ala Leu Pro Tyr Pro Ser Met Phe Pro Leu Pro Phe  
 850 855 860  
 Phe Pro Ala Phe Ser Gln Ser Met Tyr Pro Phe Pro Asp Arg Asp Leu  
 865 870 875 880  
 Arg Ser Leu Pro Leu Lys Met Glu Pro Gln Ser Pro Gly Glu Val Lys  
 885 890 895

89/299

Lys Leu Gln Lys Gly Ser Ser Glu Ser Pro Phe Asp Leu Thr Thr Lys  
 900 905 910  
 Arg Lys Asp Glu Lys Pro Leu Thr Pro Val Pro Ser Lys Pro Pro Val  
 915 920 925  
 Thr Pro Ala Thr Ser Gln Asp Gln Pro Leu Asp Leu Ser Met Gly Ser  
 930 935 940  
 Arg Ser Arg Ala Ser Gly Thr Lys Leu Thr Glu Pro Arg Lys Asn His  
 945 950 955 960  
 Val Phe Gly Gly Lys Lys Gly Ser Asn Val Glu Ser Arg Pro Ala Ser  
 965 970 975  
 Asp Gly Ser Leu Gln His Ala Arg Pro Thr Pro Phe Phe Met Asp Pro  
 980 985 990  
 Ile Tyr Arg Val Glu Lys Arg Lys Leu Thr Asp Pro Leu Glu Ala Leu  
 995 1000 1005  
 Lys Glu Lys Tyr Leu Arg Pro Ser Pro Gly Phe Leu Phe His Pro Gln  
 1010 1015 1020  
 Met Ser Ala Ile Glu Asn Met Ala Glu Lys Leu Glu Ser Phe Ser Ala  
 1025 1030 1035 1040  
 Leu Lys Pro Glu Ala Ser Glu Leu Leu Gln Ser Val Pro Ser Met Phe  
 1045 1050 1055  
 Asn Phe Arg Ala Pro Pro Asn Ala Leu Pro Glu Asn Leu Leu Arg Lys  
 1060 1065 1070  
 Gly Lys Glu Arg Tyr Thr Cys Arg Tyr Cys Gly Lys Ile Phe Pro Arg  
 1075 1080 1085  
 Ser Ala Asn Leu Thr Arg His Leu Arg Thr His Thr Gly Glu Gln Pro  
 1090 1095 1100  
 Tyr Arg Cys Lys Tyr Cys Asp Arg Ser Phe Ser Ile Ser Ser Asn Leu  
 1105 1110 1115 1120  
 Gln Arg His Val Arg Asn Ile His Asn Lys Glu Lys Pro Phe Lys Cys  
 1125 1130 1135  
 His Leu Cys Asp Arg Cys Phe Gly Gln Gln Thr Asn Leu Asp Arg His  
 1140 1145 1150  
 Leu Lys Lys His Glu Asn Gly Asn Met Ser Gly Thr Ala Thr Ser Ser  
 1155 1160 1165  
 Pro His Ser Glu Leu Glu Ser Thr Gly Ala Ile Leu Asp Asp Lys Glu  
 1170 1175 1180  
 Asp Ala Tyr Phe Thr Glu Ile Arg Asn Phe Ile Gly Asn Ser Asn His  
 1185 1190 1195 1200  
 Gly Ser Gln Ser Pro Arg Asn Val Glu Glu Arg Met Asn Gly Ser His



90/299

1205	1210	1215
Phe Lys Asp Glu Lys Ala Leu Val Thr Ser Gln Asn Ser Asp Leu Leu 1220	1225	1230
Asp Asp Glu Glu Val Glu Asp Glu Val Leu Leu Asp Glu Glu Asp Glu 1235	1240	1245
Asp Asn Asp Ile Thr Gly Lys Thr Gly Lys Glu Pro Val Thr Ser Asn 1250	1255	1260
Leu His Glu Gly Asn Pro Glu Asp Asp Tyr Glu Glu Thr Ser Ala Leu 1265	1270	1275
Glu Met Ser Cys Lys Thr Ser Pro Val Arg Tyr Lys Glu Glu Glu Tyr 1285	1290	1295
Lys Ser Gly Leu Ser Ala Leu Asp His Ile Arg His Phe Thr Asp Ser 1300	1305	1310
Leu Lys Met Arg Lys Met Glu Asp Asn Gln Tyr Ser Glu Ala Glu Leu 1315	1320	1325
Ser Ser Phe Ser Thr Ser His Val Pro Glu Glu Leu Lys Gln Pro Leu 1330	1335	1340
His Arg Lys Ser Lys Ser Gln Ala Tyr Ala Met Met Leu Ser Leu Ser 1345	1350	1355
Asp Lys Glu Ser Leu His Ser Thr Ser His Ser Ser Ser Asn Val Trp 1365	1370	1375
His Ser Met Ala Arg Ala Ala Ala Glu Ser Ser Ala Ile Gln Ser Ile 1380	1385	1390
Ser His Val 1395		

&lt;210&gt; 106

&lt;211&gt; 5938

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 106

```

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cgtgggtggt cgtgccttcg gagcagctaa ccggcggggt ctgggcgacg gtggaggagt 540
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tgccctccga agagtgcgtg tttgcatgtg tgtgactctg cggctgctca actcccaaca 660
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```

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92/299

```

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```

&lt;210&gt; 107

&lt;211&gt; 261

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 107

```

Met Asn Pro Ser Arg Asp Val His Asp Ala Ser Thr Ser Arg Arg Phe
 1              5              10              15

Thr Pro Pro Ser Thr Ala Leu Ser Pro Gly Lys Met Ser Glu Ala Leu
      20              25              30

Pro Leu Gly Ala Pro Asp Ala Gly Ala Ala Leu Ala Gly Lys Leu Arg
      35              40              45

Ser Gly Asp Arg Ser Met Val Glu Val Leu Ala Asp His Pro Gly Glu
      50              55              60

Leu Val Arg Thr Asp Ser Pro Asn Phe Leu Cys Ser Val Leu Pro Thr
      65              70              75              80

His Trp Arg Cys Asn Lys Thr Leu Pro Ile Ala Phe Lys Val Val Ala
      85              90              95

Leu Gly Asp Val Pro Asp Gly Thr Leu Val Thr Val Met Ala Gly Asn
      100              105              110

Asp Glu Asn Tyr Ser Ala Glu Leu Arg Asn Ala Thr Ala Ala Met Lys

```

93/299

115	120	125
Asn Gln Val Ala Arg Phe	Asn Asp Leu Arg Phe	Val Gly Arg Ser Gly
130	135	140
Arg Gly Lys Ser Phe Thr	Leu Thr Ile Thr Val	Phe Thr Asn Pro Pro
145	150	155
Gln Val Ala Thr Tyr His	Arg Ala Ile Lys Ile	Thr Val Asp Gly Pro
165	170	175
Arg Glu Pro Arg Arg His	Arg Gln Lys Leu Asp	Asp Gln Thr Lys Pro
180	185	190
Gly Ser Leu Ser Phe Ser	Glu Arg Leu Ser Glu	Leu Glu Gln Leu Arg
195	200	205
Arg Thr Ala Met Arg Val	Ser Pro His His Pro	Ala Pro Thr Pro Asn
210	215	220
Pro Arg Ala Ser Leu Asn	His Ser Thr Ala Phe	Asn Pro Gln Pro Gln
225	230	235
Ser Gln Met Gln Glu Ser	Trp Met Leu Pro Ile	Leu Ser Ser Phe Cys
245	250	255
Lys Lys Gly Ser Lys		
260		

&lt;210&gt; 108

&lt;211&gt; 1025

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 108

```

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gctgccctgg ccggcaagct gaggagcggc gaccgcagca tgggtggaggt gctggccgac 180
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attaa                                     1025

```

&lt;210&gt; 109

&lt;211&gt; 470

94/299

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 109

```
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ggaaaagctg ggaaccttgg tggaggggtg gtgaccatcg aaaggagcaa gagcaagatc 240
accgtgacat ccgaggtgcc tttctccaaa aggtatttga aatatctcac caaaaaatat 300
ttgaagaaga ataatctacg tgactgggtg cgcgtagttg ctaacagcaa agagagttac 360
gaattacgtt acttccagat taaccaggac gaagaagagg aggaagacga ggattaaatt 420
tcatttatct ggaaaatttt gtatgagttc ttgaataaaa cttgggaacc 470
```

&lt;210&gt; 110

&lt;211&gt; 17

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 110

```
Gly Met Gly Gly Ser Asp Arg Gly Gly Phe Asn Lys Phe Gly Gly Ser
  1                      5                      10                      15
```

Gly

&lt;210&gt; 111

&lt;211&gt; 55

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 111

```
gtggcatggg cggaagtgac cgtgggtggct tcaataaatt tggtagcagt ggcca 55
```

&lt;210&gt; 112

&lt;211&gt; 32

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 112

```
Gly Met Gly Arg Trp Lys Leu His Val Leu Ser Ser Asn Leu Ser Ser
  1                      5                      10                      15
```

```
Pro Ala Glu Val Thr Val Val Ala Ser Ile Asn Leu Val Ala Val Ala
      20                      25                      30
```

&lt;210&gt; 113

&lt;211&gt; 99

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 113

```
gtggcatggg ccgttgaag cttcatgtcc tttcttctaa cttgtcttct ccagcggag 60
tgaccgtggg ggcttcaata aatttgggtg cagtggcca 99
```

```
<210> 114
<211> 120
<212> DNA
<213> Homo sapiens
```

```
<210> 115  
<211> 375  
<212> PRT  
<213> Homo sapiens
```

<400> 115															
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1				5					10					15	
Pro	Ala	Ser	Glu	Lys	Glu	Pro	Glu	Met	Pro	Gly	Pro	Arg	Glu	Glu	Ser
			20					25					30		
Glu	Glu	Glu	Glu	Asp	Glu	Asp	Asp	Glu	Glu	Glu	Glu	Glu	Glu	Glu	Lys
		35					40					45			
Glu	Lys	Ser	Leu	Ile	Val	Glu	Gly	Lys	Arg	Glu	Lys	Lys	Lys	Val	Glu
	50					55					60				
Arg	Leu	Thr	Met	Gln	Val	Ser	Ser	Leu	Gln	Arg	Glu	Pro	Phe	Thr	Ile
65					70					75					80
Ala	Gln	Gly	Lys	Gly	Gln	Lys	Leu	Cys	Glu	Ile	Glu	Arg	Ile	His	Phe
				85					90					95	
Phe	Leu	Ser	Lys	Lys	Lys	Thr	Asp	Glu	Leu	Arg	Asn	Leu	His	Lys	Leu
			100					105					110		
Leu	Tyr	Asn	Arg	Pro	Gly	Thr	Val	Ser	Ser	Leu	Lys	Lys	Asn	Val	Gly
		115					120					125			
Gln	Phe	Ser	Gly	Phe	Pro	Phe	Glu	Lys	Gly	Ser	Val	Gln	Tyr	Lys	Lys
	130					135					140				
Lys	Glu	Glu	Met	Leu	Lys	Lys	Phe	Arg	Asn	Ala	Met	Leu	Lys	Ser	Ile
145				150						155					160
Cys	Glu	Val	Leu	Asp	Leu	Glu	Arg	Ser	Gly	Val	Asn	Ser	Glu	Leu	Val
				165					170					175	
Lys	Arg	Ile	Leu	Asn	Phe	Leu	Met	His	Pro	Lys	Pro	Ser	Gly	Lys	Pro
			180					185					190		
Leu	Pro	Lys	Ser	Lys	Lys	Thr	Cys	Ser	Lys	Gly	Ser	Lys	Lys	Glu	Arg
		195					200					205			
Asn	Ser	Ser	Gly	Met	Ala	Arg	Lys	Ala	Lys	Arg	Thr	Lys	Cys	Pro	Glu
	210					215					220				

96/299

Ile Leu Ser Asp Glu Ser Ser Ser Asp Glu Asp Glu Lys Lys Asn Lys  
 225 230 235 240  
 Glu Glu Ser Ser Asp Asp Glu Asp Lys Glu Ser Glu Glu Glu Pro Pro  
 245 250 255  
 Lys Lys Thr Ala Lys Arg Glu Lys Pro Lys Gln Lys Ala Thr Ser Lys  
 260 265 270  
 Ser Lys Lys Ser Val Lys Ser Ala Asn Val Lys Lys Ala Asp Ser Ser  
 275 280 285  
 Thr Thr Lys Lys Asn Gln Asn Ser Ser Lys Lys Glu Ser Glu Ser Glu  
 290 295 300  
 Asp Ser Ser Asp Asp Glu Pro Leu Ile Lys Lys Leu Lys Lys Pro Pro  
 305 310 315 320  
 Thr Asp Glu Glu Leu Lys Glu Thr Ile Lys Lys Leu Leu Ala Ser Ala  
 325 330 335  
 Asn Leu Glu Glu Val Thr Met Lys Gln Ile Cys Lys Lys Val Tyr Glu  
 340 345 350  
 Asn Tyr Pro Thr Tyr Asp Leu Thr Glu Arg Lys Asp Phe Ile Lys Thr  
 355 360 365  
 Thr Val Lys Glu Leu Ile Ser  
 370 375

&lt;210&gt; 116

&lt;211&gt; 2699

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; modified\_base

&lt;222&gt; (1740)

&lt;223&gt; a, c, t, g, other or unknown

&lt;400&gt; 116

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 gaggagagcg aggaggaaga ggacgaggac gacgaggagg aggaggagga ggaaaaagaa 180  
 aagagtctca tcgtggaagg caagagggaa aagaaaaaag tagagagggt gacaatgcaa 240  
 gtctcttcct tacagagaga gccatttaca attgcacaag gaaaggggca gaaactttgt 300  
 gaaattgaga ggatacattt ttttctaagt aagaagaaaa ccgatgaact tagaaatcta 360  
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 accaagaaga atcaaaacag ttccaaaaaa gaaagtgagt ctgaggatag ttcagatgat 960

97/299

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gaaccttttaa ttaaaaagtt gaagaaaccc cctacagatg aagagttaaa ggaaacaata 1020
aagaaattac tggccagtgc taacttggaa gaagtcacaa tgaaacagat ttgcaaaaag 1080
gtctatgaaa attatcctac ttatgattta actgaaagaa aagatttcat aaaaacaact 1140
gtaaaagagc taatttccttg agatagagga cagagaagat gactcgttcc catagatttg 1200
aagatctgat ttataccatt ataccagcaa agagaatgta tttccttttc taaatccttg 1260
ttaagcaacg ttagtagaac ttactgctga cctttttatc ttgagtgtta tgtgaatttg 1320
agtttgctgt tttaaattgc atttctatgc catttttagt ttaaaatcct gcatggcatt 1380
aattgttcct tgcttttata gttgtatttt gtacattttg gatttcttta tataaggtca 1440
tagattccttg agctgttggt gtttttagtg cacttaatat tagcttgctt aaggcatact 1500
tttaatcaag tagaacaaaa actattatca ccaggattta tacatacaga gattgtagta 1560
ttagtatat gaaatatttt gaatacacat ctctgtcagt gtgaaaattc agcggcagtg 1620
tgtccatcat attaaaaata tacaagctac agttgtccag atcactgaat tggaaacttt 1680
ctcctgcata tgtatatatg tcaaattgtc agcatgacaa aagtgcacaga tgttattttt 1740
gtatttttaa aaaacaattg gttgtatata aagttttttt atttcttttg tgcagatcac 1800
tttttaaaact cacataggta ggtatcttta tagttgtaga ctatggaatg tcagtgttca 1860
gccaaacagt atgatggaac agtgaaagtc aattcagtga tggcaacact gaaggaacag 1920
ttaccctgct ttgcctcgaa agtgtcatca atttghtaatt ttagtattaa ctctgtaaaa 1980
gtgtctgtag gtacgtttta tattatataa ggacagacca aaaatcaacc tatcaaagct 2040
tcaaaaactt tgggaaagggt tgggattaag tacaagcaca tttggcttac agtaaataag 2100
ctgattttta ttaactgctt ttgcccatat aaaatgctga tatttactgg aaacctagcc 2160
agcttcacga ttatgactaa agtaccagat tataatgcca gaataataatg tgcaggcaat 2220
cgtggatgtc ttgcacaaag tgtgtctcaa aaataatata cttttacatt aaagaaattt 2280
aatgtttctc tggagttggg gctcttggtc ttcagagttt gggttaatcag tgttgattct 2340
agatgatcaa cataatggac cactcctgaa tgagacttaa ttttgtcttt caaatttact 2400
gtcttaaatc agttttattaa atctgaattt taaaacatgc tgtttatgac acaatgacac 2460
atttgttgca ccaattaagt gttgaaaaat atctttgcat catagaacag aaatatataa 2520
aaatatatgt tgaatgttaa caggatattt cacaggtttg tttcttgata gttactcaga 2580
cactagggaa aggtaaatac aagtgaacaa aataagcaac taaatgagac ctaataattg 2640
gccttcgatt ttaaatattt gttcttataa acctgtgcaa taaaaataaa tctaaatca 2699

```

&lt;210&gt; 117

&lt;211&gt; 288

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 117

```

gtcaacagtc gccc aaaatt taaataaaat tattgcaggc ctataataag ttaaataagct 60
aaaattttta ataatgacag attcagtttt tagtgctgac agtgttcttt gattttgcaa 120
acaaatgagc atttctcaa tgggaagacg tcttatatgt tctatgctgt gaatagatag 180
gtttagaatt actttcagca ccgttttgct tccattacag ttaattttat ggggtgggaga 240
gcaaaatcta aatggatgca ctgtctgagt accagaatga atggaaaa 288

```

&lt;210&gt; 118

&lt;211&gt; 277

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 118

```

Met Ser Ala Gln Ala Ala Lys Val Ser Lys Lys Glu Leu Asn Ser Asn
  1                      5                      10                     15

His Asp Gly Ala Asp Glu Thr Ser Glu Lys Glu Gln Gln Glu Ala Ile
                20                      25                      30

Glu His Ile Asp Glu Val Gln Asn Glu Ile Asp Arg Leu Asn Glu Gln
  35                      40                      45

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98/299

Ala Ser Glu Glu Ile Leu Lys Val Glu Gln Lys Tyr Asn Lys Leu Arg  
 50 55 60  
 Gln Pro Phe Phe Gln Lys Arg Ser Glu Leu Ile Ala Lys Ile Pro Asn  
 65 70 75 80  
 Phe Trp Val Thr Thr Phe Val Asn His Pro Gln Val Ser Ala Leu Leu  
 85 90 95  
 Gly Glu Glu Asp Glu Glu Ala Leu His Tyr Leu Thr Arg Val Glu Val  
 100 105 110  
 Thr Glu Phe Glu Asp Ile Lys Ser Gly Tyr Arg Ile Asp Phe Tyr Phe  
 115 120 125  
 Asp Glu Asn Pro Tyr Phe Glu Asn Lys Val Leu Ser Lys Glu Phe His  
 130 135 140  
 Leu Asn Glu Ser Gly Asp Pro Ser Ser Lys Ser Thr Glu Ile Lys Trp  
 145 150 155 160  
 Lys Ser Gly Lys Asp Leu Thr Lys Arg Ser Ser Gln Thr Gln Asn Lys  
 165 170 175  
 Ala Ser Arg Lys Arg Gln His Glu Glu Pro Glu Ser Phe Phe Thr Trp  
 180 185 190  
 Phe Thr Asp His Ser Asp Ala Gly Ala Asp Glu Leu Gly Glu Val Ile  
 195 200 205  
 Lys Asp Asp Ile Trp Pro Asn Pro Leu Gln Tyr Tyr Leu Val Pro Asp  
 210 215 220  
 Met Asp Asp Glu Glu Gly Glu Gly Glu Glu Asp Asp Asp Asp Asp Glu  
 225 230 235 240  
 Glu Glu Glu Gly Leu Glu Asp Ile Asp Glu Glu Gly Asp Glu Asp Glu  
 245 250 255  
 Gly Glu Glu Asp Glu Asp Asp Asp Glu Gly Glu Glu Gly Glu Glu Asp  
 260 265 270  
 Glu Gly Glu Asp Asp  
 275

&lt;210&gt; 119

&lt;211&gt; 2577

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 119

cacatgtcgg cgcaggcggc caaagtcagt aaaaaggagc tcaactccaa ccacgacggg 60  
 gccgacgaga cctcagaaaa agaacagcaa gaagcgattg aacacattga tgaagtacaa 120  
 aatgaaatag acagacttaa tgaacaagcc agtgaggaga ttttgaaagt agaacagaaa 180  
 tataacaaac tccgccaacc attttttcag aagagggtcag aattgatcgc caaatccca 240  
 aatttttggg taacaacatt tgtcaaccat ccacaagtgt ctgcactgct tggggaggaa 300

99/299

```

gatgaagagg cactgcatta tttgaccaga gttgaagtga cagaatttga agatattaaa 360
tcaggttaca gaatagatatt ttattttgat gaaaatcctt actttgaaaa taaagttctc 420
tccaaagaat ttcacttgaa tgagagtggg gatccatctt cgaagtccac cgaaatcaaa 480
tggaaatctg gaaaggattt gacgaaacgt tcgagtcaaa cgcagaataa agccagcagg 540
aagaggcagc atgaggaacc agagagcttc tttacctggg ttactgacca ttctgatgca 600
gggtgctgat agttaggaga ggtcatcaaa gatgatattt ggccaaaccc attacagtac 660
tacttggttc ccgatatgga tgatgaagaa ggagaaggag aagaagatga tgatgatgat 720
gaagaggagg aaggattaga agatattgac gaagaagggg atgaggatga aggtgaagaa 780
gatgaagatg atgatgaagg ggaggaagga gaggaggatg aaggagaaga tgactaaata 840
gaacactgat ggattccaac cttccttttt ttaaattttt tccagtcctt gggagcaagt 900
tgcagtcctt tttttttttt tttttttttt cctctctgtg ctgagtcgcc ctgttcttga 960
ggctctcttt ctctactcca tggttctcaa tttatttggg gggaaatacc ttgagcagaa 1020
tacaatggga aaagagtctc tacccttttc gtctcgaagt tcatttttat ccttctctgt 1080
ctgaacaaaa actgtatgga atcaacacca ccgagctctg tgggaaaaaa gaaaaactgt 1140
ctccctttgc tctgctggaa gctggagggt gctaggcccc tgtgtagtag tgtatagaat 1200
tctagctttt ttctctcttt ctctgtatat tgggctcaga gactacactg tgtctctatg 1260
tgaatatgga cagttagcat ttaccaacat gtatctgtct actttctctt gtttaaaaaa 1320
agaaaaaaaa acttaaaaaa atggggttat agaagggtcag caaaggggtg ggggttgaga 1380
tgtttgggtg ggtagtggtg cattttgaca acatggcttc tcctttggca tgtttaattg 1440
tgatatttga cagacatcct tgcagtttaa gatgacactt taaaataaaa ttctctccta 1500
atgatgactt gagccctgcc actcaatggg agaatcagca gaacctgtag gatcttattt 1560
ggaattgaca ttctctattg taattttgtt cctgtttatt tttgggtttc tttttgtttc 1620
actggaaagg aaagatgatg ctgagtttta aacgttaaaa gtgtacaagt tgctttgtta 1680
caataaaact aaatgtgtac acaaaggatt tgatgctttt ctctcagcat aggtatgctt 1740
actatgacct tccaagtttg acttgataaa catcactgtc aaactttgtc accctaactt 1800
cgtatttttt gatacgcaat tttgcaggat gacctcaggg ctatgtggat tgagtaatgg 1860
gatttgaatc aatgtattaa tatctccata gctgggaaac gtgggttcaa tttgccattg 1920
gtttctgaaa agtattcaca tcatttggga taccagatag ctcaatactc tctgagtaca 1980
ttgtgccctt gatttttatc tccaagtggc agtttttaaa attggccttt tacctggata 2040
taaattaatt gtgcctgcca ccaccatcca acagacctgg tgctctaatt ccaagtata 2100
cacgggacag ttgctggcat gtcttcattg gctctctaaa atgtggccaa gaagataggc 2160
tctcagtaag aagtctgatg gtgagcagta actgtccctg ctttctggta taaagctctc 2220
aaatgtgacc atgtgaatct ggggtgggata atggactcag ctctgtctgc tcaatgccat 2280
tgtgcagaga agcaccctaa tgcataagct ttttaatgct gtaaaatata gtcgctgaaa 2340
ttaaatgcca ctttttcaga ggtgaattaa tggacagtct ggtgaacttc aaaagctttt 2400
tgatgtataa aacttgataa atggaactat tccatcaata ggcaaaagtg taacaacctc 2460
tctagatgga tagtatgtaa tttctgcaca ggtctctgtt tagtaaatac atcactgtat 2520
accgatcagg aatcttgctc caataaagga acataaagat taaaaaaaaa aaaaaaa 2577

```

&lt;210&gt; 120

&lt;211&gt; 288

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 120

```

Ala Leu Ser Leu Ala Leu Val Thr Asn Ser Ala Pro Thr Ser Ser Ser
  1                      5                      10          15

Thr Lys Lys Thr Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln
      20                      25                      30

Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg
      35                      40                      45

Met Leu Thr Phe Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys
      50                      55                      60

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100/299

His Leu Gln Cys Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu  
 65 70 75 80  
 Asn Leu Ala Gln Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile  
 85 90 95  
 Ser Asn Ile Asn Val Ile Val Leu Glu Leu Lys Met Ala Gly Gln Cys  
 100 105 110  
 Ser Gln Asn Glu Tyr Phe Asp Ser Leu Leu His Ala Cys Ile Pro Cys  
 115 120 125  
 Gln Leu Arg Cys Ser Ser Asn Thr Pro Pro Leu Thr Cys Gln Arg Tyr  
 130 135 140  
 Cys Asn Ala Ser Val Thr Asn Ser Val Lys Gly Thr Asn Ala Ile Leu  
 145 150 155 160  
 Trp Thr Cys Leu Gly Leu Ser Leu Ile Ile Ser Leu Ala Val Phe Val  
 165 170 175  
 Leu Met Phe Leu Leu Arg Lys Ile Ser Ser Glu Pro Leu Lys Asp Glu  
 180 185 190  
 Phe Lys Asn Thr Gly Ser Gly Leu Leu Gly Met Ala Asn Ile Asp Leu  
 195 200 205  
 Glu Lys Ser Arg Thr Gly Asp Glu Ile Ile Leu Pro Arg Gly Leu Glu  
 210 215 220  
 Tyr Thr Val Glu Glu Cys Thr Cys Glu Asp Cys Ile Lys Ser Lys Pro  
 225 230 235 240  
 Lys Val Asp Ser Asp His Cys Phe Pro Leu Pro Ala Met Glu Glu Gly  
 245 250 255  
 Ala Thr Ile Leu Val Thr Thr Lys Thr Asn Asp Tyr Cys Lys Ser Leu  
 260 265 270  
 Pro Ala Ala Leu Ser Ala Thr Glu Ile Glu Lys Ser Ile Ser Ala Arg  
 275 280 285

&lt;210&gt; 121

&lt;211&gt; 1073

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 121

gcactaagtc ttgcacttgt cacaaacagt gcacctactt caagttctac aaagaaaaca 60  
 cagctacaac tggagcathtt actgctggat ttacagatga ttttgaatgg aattaataat 120  
 tacaagaatc ccaaactcac caggatgctc acatttaagt tttacatgcc caagaaggcc 180  
 acagaactga aacatcttca gtgtctagaa gaagaactca aacctctgga ggaagtgcta 240  
 aatttagctc aaagcaaaaa ctttacttta agaccaggg acttaatcag caatatcaac 300  
 gtaatagttc tggaactaaa gatggctggg cagtgcctccc aaaatgaata ttttgacagt 360  
 ttgttgcatg cttgcatacc ttgtcaactt cgatgttctt ctaatactcc toctctaaca 420  
 tgtcagcgtt attgtaatgc aagtgtgacc aattcagtga aaggaacgaa tgcgattctc 480  
 tggacctgtt tgggactgag cttaataatt tctttggcag ttttcgtgct aatgtttttg 540

101/299

```

ctaaggaaga taagctctga accattaaag gacgagttta aaaacacagg atcaggtctc 600
ctgggcatgg ctaacattga cctggaaaag agcaggactg gtgatgaaat tattcttccg 660
agaggcctcg agtacacggg ggaagaatgc acctgtgaag actgcatcaa gagcaaaccg 720
aaggctcgact ctgaccattg ctttccactc ccagctatgg aggaaggcgc aaccattctt 780
gtcaccacga aaacgaatga ctattgcaag agcctgccag ctgctttgag tgcacggag 840
atagagaaat caatttctgc taggtaatta accatttcga ctcgagcagt gccactttaa 900
aaatcttttg tcagaataga tgatgtgtca gatctcttta ggatgactgt atttttcagt 960
tgccgatata gctttttgtc ctctaactgt ggaaactctt tatgttagat atatttctct 1020
aggttactgt tgggagctta atggtagaaa cttccttggg ttctatgatt aaa 1073

```

&lt;210&gt; 122

&lt;211&gt; 26

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 122

```

Glu Phe Glu Asp Arg Asp Arg Ser His Arg Glu Glu Met Glu Phe Lys
  1                   5                   10                   15

```

```

Arg Ala Lys Ala Asn Leu Asp Lys Asn Lys
          20                   25

```

&lt;210&gt; 123

&lt;211&gt; 78

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 123

```

gaatttgaag atagagacag gtctcatcgg gaggaatgg agttcaagag ggccaaggcg 60
aacctagaca agaataag                                     78

```

&lt;210&gt; 124

&lt;211&gt; 34

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 124

```

Glu Phe Glu Asp Arg Asp Arg Ser His Arg Glu Glu Met Glu Val His
  1                   5                   10                   15

```

```

Glu Leu Glu Lys Ser Lys Arg Ala Leu Glu Thr Gln Met Glu Glu Met
          20                   25                   30

```

Lys Thr

&lt;210&gt; 125

&lt;211&gt; 102

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 125

```

gaatttgaag atagagacag gtctcatcgg gaggaatgg aggtccatga gctggagaag 60
tccaagcggg ccctggagac ccagatggag gagatgaaga cg 102

```

102/299

&lt;210&gt; 126

&lt;211&gt; 50

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 126

Glu Phe Glu Asp Arg Asp Arg Ser His Arg Glu Glu Met Glu Asn Glu  
1 5 10 15

Val Glu Ser Val Thr Gly Met Leu Asn Glu Ala Glu Gly Lys Ala Ile  
20 25 30

Lys Leu Ala Lys Asp Val Ala Ser Leu Ser Ser Gln Leu Gln Asp Thr  
35 40 45

Gln Glu  
50

&lt;210&gt; 127

&lt;211&gt; 152

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 127

gaattttgaag atagagacag gtctcatcgg gaggaatgg agaatgaagt tgagagcgtc 60  
acaggggatgc ttaacgaggc cgaggggaag gccattaagc tggccaagga cgtggcgtcc 120  
ctcagttccc agctccagga caccaggag tt 152

&lt;210&gt; 128

&lt;211&gt; 1353

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; modified\_base

&lt;222&gt; (941)

&lt;223&gt; a, c, t, g, other or unknown

&lt;220&gt;

&lt;221&gt; modified\_base

&lt;222&gt; (1067)

&lt;223&gt; a, c, t, g, other or unknown

&lt;220&gt;

&lt;221&gt; modified\_base

&lt;222&gt; (1077)

&lt;223&gt; a, c, t, g, other or unknown

&lt;400&gt; 128

cttggccaac attctggagg cagtaaagaa agcttataga ataaccacat attagaactt 60  
gtgaaggaga aaatatacat atatatatat gtatatatat agtctctcta ttaagtaatt 120  
taccataagg ggtttaaata ggaatgtttt ctccaaagtg aatcttgaaa tcttgggtgtt 180  
tataattgtc aagcctcttt ttttaaaata gatttgggtca acaggaagta tttttttcta 240  
atttttatatt tatagaccta gtcaagcttc ttaattgtta aatattgtta taacaataca 300  
tctggggcgg gcgcgggtggc tcactcctgt aatcccagca ctttgggagg ccagggcggg 360

103/299

```

tgaatcacga ggtcaggaga ttgagaccat cctggctaac acaaagaaac cccatctcta 420
ctaaaaatac aaaaaattag ctgggagagg aggagggcgc ctgtagtccc agctactcgg 480
gaggcggagc ttgcggtgag ccaagatcgc gccactgcac tccagcgact ccgtctcaaa 540
aaaaaaaaaa aaaaaacatc tgagtcggtta catggttggt agccgaggag aaaaacatct 600
cttccaaata cgcggatgag agggacagag ctgaggcaga agccagggag aaggaaacca 660
aggccctgtc cctggctcgg gcccttgaag aggccttgga agccaaagag gaactcgagc 720
ggaccaacaa aatgctcaaa gccgaaatgg aagacctggg cagctccaag gatgacgtgg 780
gcaagaacgt aagtggctct ggggtggttt tctcgtccat gtttcgcctg cccaccctct 840
gtgctattca ccagtcocatg cgaggctagc tcctggcctt tttcatagcg aactatcatc 900
ggaaatggaa ggaggttttt ggactgggtgc aggggctaaa naggggctga gaatggcagt 960
cgaggatggg tctgagttgg ggggtccgag gataaggctg ggggtctgaac tctcaggggt 1020
catcttgatg cccggccatg catcctgtgg gaggccaaag ccacctnccc tgatctnctt 1080
gaggtgccgc tcacgggtggg tttctcaatc gtcttcatga agttgagcct catagaatgg 1140
ggctgcccgc tctgccggca ggtccatgag ctggagaagt ccaagcgggc cctggagacc 1200
cagatggagg agatgaagac gcagctggaa gagctggagg acgagctgca agccacggag 1260
gacgccaaac tgcggctgga agtcaacatg caggcgctca agggccagtt cgaaagggat 1320
ctccaagccc gggacgagca gaatgaggag aag                                     1353

```

&lt;210&gt; 129

&lt;211&gt; 744

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; modified\_base

&lt;222&gt; (326)

&lt;223&gt; a, c, t, g, other or unknown

&lt;220&gt;

&lt;221&gt; modified\_base

&lt;222&gt; (614)

&lt;223&gt; a, c, t, g, other or unknown

&lt;400&gt; 129

```

gcccggttta aaatttagta tcttttagtg attgctagat ctctttgtca gtgagttaat 60
taatctaata ggctgatagc agctgaggat gtccccaaga atacttgtaa gctaagagaa 120
gaaaatggag ggatataatg gatacttggt ttctttgatg ctggttgtaa tcttggtgatt 180
ttcatatatg tgaatacaag acttccacac catgcccttt ctttcggtat ctgtaaaatt 240
tagaagcttt aaaatgtata atgtacattt gttacatttc tgaacctttt tgctcatgct 300
ctttgttccc tgatgtagaa tggtcnattc tgtccgtcaa ggcccaacct gaatggtgtc 360
attaaatgtc aggcctttcc tcagtctctg ggggtctgaac tgctcagggg tcatcttgag 420
tcccggccat gcacctctgt ggaggccaaa gccacctccc tgatctctct aggtgccgct 480
cacggtgggt ttctcaatcg tcttcatgaa gttgagcctc atagaatggg gctgcccgct 540
ctgccggcag gtccatgagc tggagaagtc caagcggggc ctggagaccc agatggagga 600
gatgaagacg cagntggaag agctggagga cgagctgcaa gccacggagg acgccaaact 660
gcggtctgaa gtcaacatgc aggcgctcaa gggccagttc gaaagggatc tccaagcccc 720
ggacgagcag aatgaggaga agag                                     744

```

&lt;210&gt; 130

&lt;211&gt; 29

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 130

```

Arg Glu Phe Glu Asp Arg Asp Arg Ser His Arg Glu Glu Met Glu Glu
  1                      5                      10                     15

```

104/299

Leu Leu Gln Glu Glu Thr Arg Gln Lys Leu Asn Val Ser  
                   20                                  25

&lt;210&gt; 131

&lt;211&gt; 89

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 131

acgcgaattt gaagatagag acaggtctca tcgggaggaa atggaggagc tgcttcaaga 60  
 agaaacccgg cagaagctca acgtgtcta 89

&lt;210&gt; 132

&lt;211&gt; 452

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 132

Met Ser Glu Thr Pro Ala Gln Cys Ser Ile Lys Gln Glu Arg Ile Ser  
   1                  5                                  10                                  15

Tyr Thr Pro Pro Glu Ser Pro Val Pro Ser Tyr Ala Ser Ser Thr Pro  
                   20                                  25                                  30

Leu His Val Pro Val Pro Arg Ala Leu Arg Met Glu Glu Asp Ser Ile  
                   35                                  40                                  45

Arg Leu Pro Ala His Leu Arg Leu Gln Pro Ile Tyr Trp Ser Arg Asp  
   50                                  55                                  60

Asp Val Ala Gln Trp Leu Lys Trp Ala Glu Asn Glu Phe Ser Leu Arg  
   65                                  70                                  75                                  80

Pro Ile Asp Ser Asn Thr Phe Glu Met Asn Gly Lys Ala Leu Leu Leu  
                                   85                                  90                                  95

Leu Thr Lys Glu Asp Phe Arg Tyr Arg Ser Pro His Ser Gly Asp Val  
                   100                                  105                                  110

Leu Tyr Glu Leu Leu Gln His Ile Leu Lys Gln Arg Lys Pro Arg Ile  
                   115                                  120                                  125

Leu Phe Ser Pro Phe Phe His Pro Gly Asn Ser Ile His Thr Gln Pro  
                   130                                  135                                  140

Glu Val Ile Leu His Gln Asn His Glu Glu Asp Asn Cys Val Gln Arg  
   145                                  150                                  155                                  160

Thr Pro Arg Pro Ser Val Asp Asn Val His His Asn Pro Pro Thr Ile  
                                   165                                  170                                  175

Glu Leu Leu His Arg Ser Arg Ser Pro Ile Thr Thr Asn His Arg Pro  
                   180                                  185                                  190

Ser Pro Asp Pro Glu Gln Arg Pro Leu Arg Ser Pro Leu Asp Asn Met

105/299

195	200	205
Ile Arg Arg Leu Ser Pro	Ala Glu Arg Ala Gln Gly	Pro Arg Pro His
210	215	220
Gln Glu Asn Asn His	Gln Glu Ser Tyr Pro	Leu Ser Val Ser Pro Met
225	230	235 240
Glu Asn Asn His Cys	Pro Ala Ser Ser Glu	Ser His Pro Lys Pro Ser
245	250	255
Ser Pro Arg Gln Glu Ser Thr	Arg Val Ile Gln Leu Met	Pro Ser Pro
260	265	270
Ile Met His Pro Leu Ile	Leu Asn Pro Arg His	Ser Val Asp Phe Lys
275	280	285
Gln Ser Arg Leu Ser Glu	Asp Gly Leu His Arg	Glu Gly Lys Pro Ile
290	295	300
Asn Leu Ser His Arg Glu	Asp Leu Ala Tyr Met	Asn His Ile Met Val
305	310	315 320
Ser Val Ser Pro Pro Glu	Glu His Ala Met Pro	Ile Gly Arg Ile Ala
325	330	335
Asp Cys Arg Leu Leu Trp	Asp Tyr Val Tyr Gln	Leu Leu Ser Asp Ser
340	345	350
Arg Tyr Glu Asn Phe Ile	Arg Trp Glu Asp Lys	Glu Ser Lys Ile Phe
355	360	365
Arg Ile Val Asp Pro Asn	Gly Leu Ala Arg Leu	Trp Gly Asn His Lys
370	375	380
Asn Arg Thr Asn Met Thr	Tyr Glu Lys Met Ser	Arg Ala Leu Arg His
385	390	395 400
Tyr Tyr Lys Leu Asn Ile	Ile Arg Lys Glu Pro	Gly Gln Arg Leu Leu
405	410	415
Phe Arg Phe Met Lys Thr	Pro Asp Glu Ile Met	Ser Gly Arg Thr Asp
420	425	430
Arg Leu Glu His Leu Glu	Ser Gln Glu Leu Asp	Glu Gln Ile Tyr Gln
435	440	445
Glu Asp Glu Cys		
450		

&lt;210&gt; 133

&lt;211&gt; 1956

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 133

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106/299

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cacctgcgct tgcagccaat ttactggagc agggatgacg tagcccagtg gctcaagtgg 240
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tactgttggg tcttggtga aaaaaaaaa aaaaaa 1956

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&lt;210&gt; 134

&lt;211&gt; 452

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 134

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Met Ser Glu Thr Pro Ala Gln Cys Ser Ile Lys Gln Glu Arg Ile Ser
  1                      5                      10                      15

Tyr Thr Pro Pro Glu Ser Pro Val Pro Ser Tyr Ala Ser Ser Thr Pro
          20                      25                      30

Leu His Val Pro Val Pro Arg Ala Leu Arg Met Glu Glu Asp Ser Ile
          35                      40                      45

Arg Leu Pro Ala His Leu Arg Leu Gln Pro Ile Tyr Trp Ser Arg Asp
          50                      55                      60

Asp Val Ala Gln Trp Leu Lys Trp Ala Glu Asn Glu Phe Ser Leu Arg
          65                      70                      75                      80

Pro Ile Asp Ser Asn Thr Phe Glu Met Asn Gly Lys Ala Leu Leu Leu
          85                      90                      95

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107/299

Leu	Thr	Lys	Glu	Asp	Phe	Arg	Tyr	Arg	Ser	Pro	His	Ser	Gly	Asp	Val	100	105	110
Leu	Tyr	Glu	Leu	Leu	Gln	His	Ile	Leu	Lys	Gln	Arg	Lys	Pro	Arg	Ile	115	120	125
Leu	Phe	Ser	Pro	Phe	Phe	His	Pro	Gly	Asn	Ser	Ile	His	Thr	Gln	Pro	130	135	140
Glu	Val	Ile	Leu	His	Gln	Asn	His	Glu	Glu	Asp	Asn	Cys	Val	Gln	Arg	145	150	155
Thr	Pro	Arg	Pro	Ser	Val	Asp	Asn	Val	His	His	Asn	Pro	Pro	Thr	Ile	165	170	175
Glu	Leu	Leu	His	Arg	Ser	Arg	Ser	Pro	Ile	Thr	Thr	Asn	His	Arg	Pro	180	185	190
Ser	Pro	Asp	Pro	Glu	Gln	Arg	Pro	Leu	Arg	Ser	Pro	Leu	Asp	Asn	Met	195	200	205
Ile	Arg	Arg	Leu	Ser	Pro	Ala	Glu	Arg	Ala	Gln	Gly	Pro	Arg	Pro	His	210	215	220
Gln	Glu	Asn	Asn	His	Gln	Glu	Ser	Tyr	Pro	Leu	Ser	Val	Ser	Pro	Met	225	230	235
Glu	Asn	Asn	His	Cys	Pro	Ala	Ser	Ser	Glu	Ser	His	Pro	Lys	Pro	Ser	245	250	255
Ser	Pro	Arg	Gln	Glu	Ser	Thr	Arg	Val	Ile	Gln	Leu	Met	Pro	Ser	Pro	260	265	270
Ile	Met	His	Pro	Leu	Ile	Leu	Asn	Pro	Arg	His	Ser	Val	Asp	Phe	Lys	275	280	285
Gln	Ser	Arg	Leu	Ser	Glu	Asp	Gly	Leu	His	Arg	Glu	Gly	Lys	Pro	Ile	290	295	300
Asn	Leu	Ser	His	Arg	Glu	Asp	Leu	Ala	Tyr	Met	Asn	His	Ile	Met	Val	305	310	315
Ser	Val	Ser	Pro	Pro	Glu	Glu	His	Ala	Met	Pro	Ile	Gly	Arg	Ile	Ala	325	330	335
Asp	Cys	Arg	Leu	Leu	Trp	Asp	Tyr	Val	Tyr	Gln	Leu	Leu	Ser	Asp	Ser	340	345	350
Arg	Tyr	Glu	Asn	Phe	Ile	Arg	Trp	Glu	Asp	Lys	Glu	Ser	Lys	Ile	Phe	355	360	365
Arg	Ile	Val	Asp	Pro	Asn	Gly	Leu	Ala	Arg	Leu	Trp	Gly	Asn	His	Lys	370	375	380
Asn	Arg	Thr	Asn	Met	Thr	Tyr	Glu	Lys	Met	Ser	Arg	Ala	Leu	Arg	His	385	390	395
Tyr	Tyr	Lys	Leu	Asn	Ile	Ile	Arg	Lys	Glu	Pro	Gly	Gln	Arg	Leu	Leu			

108/299

	405		410		415
Phe Arg Phe Met Lys Thr Pro Asp Glu Ile Met Ser Gly Arg Thr Asp					
	420		425		430
Arg Leu Glu His Leu Glu Ser Gln Glu Leu Asp Glu Gln Ile Tyr Gln					
	435		440		445
Glu Asp Glu Cys					
450					

<210> 135  
 <211> 1580  
 <212> DNA  
 <213> Homo sapiens

<400> 135

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cttcatgttc	cagtgcctcg	agcgctcagc	atggaggaag	actcgatccg	cctgcctgcg	180
cacctgcgct	tgcagccaat	ttactggagc	agggatgacg	tagcccagtg	gctcaagtgg	240
gctgaaaatg	agttttcttt	aaggccaatt	gacagcaaca	cgtttgaaat	gaatggcaaa	300
gctctcctgc	tgctgaccaa	agaggacttt	cgctatcgat	ctcctcattc	aggtgatgtg	360
ctctatgaac	tccttcagca	tattctgaag	cagaggaaac	ctcggattct	tttttcacca	420
ttcttccacc	ctggaaactc	tatacacaca	cagccggagg	tcatactgca	tcagaaccat	480
gaagaagata	actgtgtcca	gaggaccccc	aggccatccg	tggataatgt	gcaccataac	540
cctcccacca	ttgaactggt	gcaccgctcc	aggtcaccta	tcacgacaaa	tcaccggcct	600
tctcctgacc	ccgagcagcg	gccccctcgg	tcccccttgg	acaacatgat	ccgccgcctc	660
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taccctctgt	cagtgtctcc	catggagaat	aatcactgcc	cagcgtcctc	cgagtcccac	780
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cggtacgaaa	acttcatccg	atgggaggac	aaagaatcca	aaatattccg	gatagtggat	1140
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<210> 136  
 <211> 1451  
 <212> DNA  
 <213> Homo sapiens

<400> 136

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ggtgccaaag	tgctacttcg	ttatgctagt	ccctggaatt	gggtgggggtg	gtgattaggg	180
cagcccaggc	caagccaaaa	cggaagctcc	caaccttccc	cccaccagag	cagctgcagt	240
tccctgagga	gcccctgatt	ctgcacctca	gccccgtgtg	tatcctcctg	gctgatcagg	300

109/299

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gggtgggggag ctcccttcagt gtccatcacg atggtgaaag ctcgcccccac cccctagacg 360
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aatgcactag ccactcttc cccaaaccag cccctccacca ccctccaggc agagagatag 480
gaaaatcggg ttctgagtat atttctgttc agcctgtgag ccaagggtgag ctgacctgca 540
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gacagatggg cagaggcttg aaaagggcag agggaaaggc tcttgagagc cctcgaggc 660
caggccctg caggcaaagg gatctgccgg tagaaggagg atggcagcac acactgtgtc 720
cccatatggg gccatccctc aaagggacag gataatagga gctaacactt gttgcatggt 780
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cggctctgccc c

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&lt;210&gt; 137

&lt;211&gt; 1565

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 137

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gagctgcaag ccatgcagat ggagctgcag agccctgagt acaagctgag caagtcgcga 1560
cctcg

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&lt;210&gt; 138

110/299

&lt;211&gt; 1679

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 138

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caagccatgc agatggagct gcagagccct gagtacaagc tgagcaagtc cgcacctcg 1679

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&lt;210&gt; 139

&lt;211&gt; 680

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 139

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Met Glu Asp Ser Met Asp Met Asp Met Ser Pro Leu Arg Pro Gln Asn
  1                      5                      10                      15

Tyr Leu Phe Gly Cys Glu Leu Lys Ala Asp Lys Asp Tyr His Phe Lys
      20                      25                      30

Val Asp Asn Asp Glu Asn Glu His Gln Leu Ser Leu Arg Thr Val Ser
      35                      40                      45

Leu Gly Ala Gly Ala Lys Asp Glu Leu His Ile Val Glu Ala Glu Ala
      50                      55                      60

Met Asn Tyr Glu Gly Ser Pro Ile Lys Val Thr Leu Ala Thr Leu Lys
      65                      70                      75                      80

Met Ser Val Gln Pro Thr Val Ser Leu Gly Gly Phe Glu Ile Thr Pro
      85                      90                      95

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111/299

Pro	Val	Val	Leu	Arg	Leu	Lys	Cys	Gly	Ser	Gly	Pro	Val	His	Ile	Ser	
			100					105						110		
Gly	Gln	His	Leu	Val	Val	Tyr	Arg	Arg	Lys	His	Gln	Glu	Leu	Gln	Ala	
		115					120					125				
Met	Gln	Met	Glu	Leu	Gln	Ser	Pro	Glu	Tyr	Lys	Leu	Ser	Lys	Leu	Arg	
	130					135					140					
Thr	Ser	Thr	Ile	Met	Thr	Asp	Tyr	Asn	Pro	Asn	Tyr	Cys	Phe	Ala	Gly	
145					150					155					160	
Lys	Thr	Ser	Ser	Ile	Ser	Asp	Leu	Lys	Glu	Val	Pro	Arg	Lys	Asn	Ile	
				165					170					175		
Thr	Leu	Ile	Arg	Gly	Leu	Gly	His	Gly	Ala	Phe	Gly	Glu	Val	Tyr	Glu	
			180					185					190			
Gly	Gln	Val	Ser	Gly	Met	Pro	Asn	Asp	Pro	Ser	Pro	Leu	Gln	Val	Ala	
	195						200					205				
Val	Lys	Thr	Leu	Pro	Glu	Val	Cys	Ser	Glu	Gln	Asp	Glu	Leu	Asp	Phe	
	210					215					220					
Leu	Met	Glu	Ala	Leu	Ile	Ile	Ser	Lys	Phe	Asn	His	Gln	Asn	Ile	Val	
225					230					235					240	
Arg	Cys	Ile	Gly	Val	Ser	Leu	Gln	Ser	Leu	Pro	Arg	Phe	Ile	Leu	Leu	
				245					250					255		
Glu	Leu	Met	Ala	Gly	Gly	Asp	Leu	Lys	Ser	Phe	Leu	Arg	Glu	Thr	Arg	
		260						265					270			
Pro	Arg	Pro	Ser	Gln	Pro	Ser	Ser	Leu	Ala	Met	Leu	Asp	Leu	Leu	His	
		275					280					285				
Val	Ala	Arg	Asp	Ile	Ala	Cys	Gly	Cys	Gln	Tyr	Leu	Glu	Glu	Asn	His	
	290					295					300					
Phe	Ile	His	Arg	Asp	Ile	Ala	Ala	Arg	Asn	Cys	Leu	Leu	Thr	Cys	Pro	
305					310					315					320	
Gly	Pro	Gly	Arg	Val	Ala	Lys	Ile	Gly	Asp	Phe	Gly	Met	Ala	Arg	Asp	
				325					330				335			
Ile	Tyr	Arg	Ala	Ser	Tyr	Tyr	Arg	Lys	Gly	Gly	Cys	Ala	Met	Leu	Pro	
			340					345					350			
Val	Lys	Trp	Met	Pro	Pro	Glu	Ala	Phe	Met	Glu	Gly	Ile	Phe	Thr	Ser	
		355					360					365				
Lys	Thr	Asp	Thr	Trp	Ser	Phe	Gly	Val	Leu	Leu	Trp	Glu	Ile	Phe	Ser	
	370					375					380					
Leu	Gly	Tyr	Met	Pro	Tyr	Pro	Ser	Lys	Ser	Asn	Gln	Glu	Val	Leu	Glu	
385					390					395					400	

112/299

Phe Val Thr Ser Gly Gly Arg Met Asp Pro Pro Lys Asn Cys Pro Gly  
 405 410 415  
 Pro Val Tyr Arg Ile Met Thr Gln Cys Trp Gln His Gln Pro Glu Asp  
 420 425 430  
 Arg Pro Asn Phe Ala Ile Ile Leu Glu Arg Ile Glu Tyr Cys Thr Gln  
 435 440 445  
 Asp Pro Asp Val Ile Asn Thr Ala Leu Pro Ile Glu Tyr Gly Pro Leu  
 450 455 460  
 Val Glu Glu Glu Glu Lys Val Pro Val Arg Pro Lys Asp Pro Glu Gly  
 465 470 475 480  
 Val Pro Pro Leu Leu Val Ser Gln Gln Ala Lys Arg Glu Glu Glu Arg  
 485 490 495  
 Ser Pro Ala Ala Pro Pro Pro Leu Pro Thr Thr Ser Ser Gly Lys Ala  
 500 505 510  
 Ala Lys Lys Pro Thr Ala Ala Glu Val Ser Val Arg Val Pro Arg Gly  
 515 520 525  
 Pro Ala Val Glu Gly Gly His Val Asn Met Ala Phe Ser Gln Ser Asn  
 530 535 540  
 Pro Pro Ser Glu Leu His Lys Val His Gly Ser Arg Asn Lys Pro Thr  
 545 550 555 560  
 Ser Leu Trp Asn Pro Thr Tyr Gly Ser Trp Phe Thr Glu Lys Pro Thr  
 565 570 575  
 Lys Lys Asn Asn Pro Ile Ala Lys Lys Glu Pro His Asp Arg Gly Asn  
 580 585 590  
 Leu Gly Leu Glu Gly Ser Cys Thr Val Pro Pro Asn Val Ala Thr Gly  
 595 600 605  
 Arg Leu Pro Gly Ala Ser Leu Leu Leu Glu Pro Ser Ser Leu Thr Ala  
 610 615 620  
 Asn Met Lys Glu Val Pro Leu Phe Arg Leu Arg His Phe Pro Cys Gly  
 625 630 635 640  
 Asn Val Asn Tyr Gly Tyr Gln Gln Gln Gly Leu Pro Leu Glu Ala Ala  
 645 650 655  
 Thr Ala Pro Gly Ala Gly His Tyr Glu Asp Thr Ile Leu Lys Ser Lys  
 660 665 670  
 Asn Ser Met Asn Gln Pro Gly Pro  
 675 680

&lt;210&gt; 140

&lt;211&gt; 2043

&lt;212&gt; DNA

113/299

&lt;213&gt; Homo sapiens

&lt;400&gt; 140

```

atggaagatt cgatggacat ggacatgagc cccctgaggc cccagaacta tcttttcggt 60
tgtgaactaa aggccgacaa agattatcac ttttaagggtg ataatgatga aaatgagcac 120
cagttatctt taagaacggt cagtttaggg gctggtgcaa aggatgagtt gcacattggt 180
gaagcagagg caatgaatta cgaaggcagt ccaattaaag taacactggc aactttgaaa 240
atgtctgtac agccaacggt ttcccttggg ggctttgaaa taacaccacc agtgggtctta 300
aggttgaagt gtggttcagg gccagtgcac attagtggac agcacttagt agtgtagcgc 360
cggaagcacc aggagctgca agccatgcag atggagctgc agagccctga gtacaagctg 420
agcaagctcc gcacctcgac catcatgacc gactacaacc ccaactactg ctttgctggc 480
aagacctcc ccatcagtga cctgaaggag gtgccgcgga aaaacatcac cctcattcgg 540
ggctctggcc atggcgccct tggggagggt tatgaaggcc aggtgtccgg aatgccaac 600
gaccaagcc cctgcaagt ggctgtgaag acgctgcctg aagtgtgctc tgaacaggac 660
gaactggatt tcctcatgga agccctgatc atcagcaaata tcaaccacca gaacattggt 720
cgctgcattg gggtagcctt gcaatccctg ccccggttca tcctgctgga gctcatggcg 780
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aatgtcaatt acggctacca gcaacagggc ttgcccttag aagccgctac tgcccctgga 1980
gctggtcatt acgaggatac cattctgaaa agcaagaata gcatgaacca gcctggggcc 2040
tga 2043

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&lt;210&gt; 141

&lt;211&gt; 180

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 141

```

caggaccacc ccagtagcat ggggtgtttat gggcaggagt ctggaggatt ttccggacca 60
ggagagaacc ggagcatgag tggccctgca tggaggacac ataaagggtt cctggagggt 120
gacaatcaca gttaccctct catactcaca tgcaaggacg aggaacttgt ttccatttac 180

```

&lt;210&gt; 142

&lt;211&gt; 180

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 142

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aaggttgtat attgaggaata tttgagcaag ctgccctgaa gaaaggcata gtgacaagat 60

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114/299

gagagagatg cattgttttg agatgtgttt agccagtgcc cttcttcccc acgatcaggt 120  
 tcctggagct taggatgtgt gatgcagaag aagtctggaa aggtaagaaa cagaattgta 180

&lt;210&gt; 143

&lt;211&gt; 427

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 143

tcaatggcac tctcatccct tagcatcagg ctcaagctcc tgagaagcag caggacttaa 60  
 ctcaactctgc cttcacagtc agcagccact ctctcagagc tgggtgtggga atccaaagtg 120  
 aataaatcag agccctcaag acactgaatg ccaggagcat ggtctgaggg acagtgtgct 180  
 ataatagaga tacatatgga ggaagcggag gaggaaggag cagattgtgt ttgagaatgg 240  
 cttaagcaga gttgaagcta tttctcaggg ttatcaactt ccaccagagg aactggaatt 300  
 tgttgtatatt ctctataaat attgatgggt aacatttatg tttagaaatc tcctcttagt 360  
 gcctttacat tactaaacat taagagatga ttgaagggaa aatgcacttt agaccaggtg 420  
 aaattag 427

&lt;210&gt; 144

&lt;211&gt; 438

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 144

gatccactca tcagagggga gtccacagtc cccacagagg gccggcatgt gtgggaggtt 60  
 aggaaatgtc agcactgccc tgaaacaaat caggcgtggc ccttgccgag cacctggcac 120  
 atagtaggtg ctaaataaat atttgttgaa tggatgaatt gttaggtaag tagaaataga 180  
 gagataggta ggtaggtagg taggtaggta ggtagataga tagagacaga taaataaatg 240  
 ggttgacaga tgtgtggatt ggatgagtgg atgggtgagt tgggtggatag atggattgga 300  
 ttgtatagat gaattgaatg gatggttgaa tggatggata gatggatgga tgggtggaat 360  
 agatggatgg acggatggat ggatggatgg atggatggat ggatggatga tgkatggatg 420  
 gacggacaga cggacgga 438

&lt;210&gt; 145

&lt;211&gt; 135

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 145

gtactagata gtgtcccact tggcccaact acgacatgca gaaaccaaca atgccaaccc 60  
 ttggagctag accttgatt caggagcttg atcccctaca actgctctgg tatgtcaata 120  
 tacctcttcg gatga 135

&lt;210&gt; 146

&lt;211&gt; 476

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 146

Met Ala Ser Thr Asp Tyr Ser Thr Tyr Ser Gln Ala Ala Ala Gln Gln  
 1 5 10 15  
 Gly Tyr Ser Ala Tyr Thr Ala Gln Pro Thr Gln Gly Tyr Ala Gln Thr  
 20 25 30

115/299

Thr Gln Ala Tyr Gly Gln Gln Ser Tyr Gly Thr Tyr Gly Gln Pro Thr  
 35 40 45  
 Asp Val Ser Tyr Thr Gln Ala Gln Thr Thr Ala Thr Tyr Gly Gln Thr  
 50 55 60  
 Ala Tyr Ala Thr Ser Tyr Gly Gln Pro Pro Thr Gly Tyr Thr Thr Pro  
 65 70 75 80  
 Thr Ala Pro Gln Ala Tyr Ser Gln Pro Val Gln Gly Tyr Gly Thr Gly  
 85 90 95  
 Ala Tyr Asp Thr Thr Thr Ala Thr Val Thr Thr Thr Gln Ala Ser Tyr  
 100 105 110  
 Ala Ala Gln Ser Ala Tyr Gly Thr Gln Pro Ala Tyr Pro Ala Tyr Gly  
 115 120 125  
 Gln Gln Pro Ala Ala Thr Ala Pro Thr Arg Pro Gln Asp Gly Asn Lys  
 130 135 140  
 Pro Thr Glu Thr Ser Gln Pro Gln Ser Ser Thr Gly Gly Tyr Asn Gln  
 145 150 155 160  
 Pro Ser Leu Gly Tyr Gly Gln Ser Asn Tyr Ser Tyr Pro Gln Val Pro  
 165 170 175  
 Gly Ser Tyr Pro Met Gln Pro Val Thr Ala Pro Pro Ser Tyr Pro Pro  
 180 185 190  
 Thr Ser Tyr Ser Ser Thr Gln Pro Thr Ser Tyr Asp Gln Ser Ser Tyr  
 195 200 205  
 Ser Gln Gln Asn Thr Tyr Gly Gln Pro Ser Ser Tyr Gly Gln Gln Ser  
 210 215 220  
 Ser Tyr Gly Gln Gln Ser Ser Tyr Gly Gln Gln Pro Pro Thr Ser Tyr  
 225 230 235 240  
 Pro Pro Gln Thr Gly Ser Tyr Ser Gln Ala Pro Ser Gln Tyr Ser Gln  
 245 250 255  
 Gln Ser Ser Ser Tyr Gly Gln Gln Ser Pro Pro Leu Gly Gly Ala Gln  
 260 265 270  
 Thr Ile Ser Lys Asn Thr Glu Gln Arg Pro Gln Pro Asp Pro Tyr Gln  
 275 280 285  
 Ile Leu Gly Pro Thr Ser Ser Arg Leu Ala Asn Pro Gly Ser Gly Gln  
 290 295 300  
 Ile Gln Leu Trp Gln Phe Leu Leu Glu Leu Leu Ser Asp Ser Ala Asn  
 305 310 315 320  
 Ala Ser Cys Ile Thr Trp Glu Gly Thr Asn Gly Glu Phe Lys Met Thr  
 325 330 335

116/299

Asp Pro Asp Glu Val Ala Arg Arg Trp Gly Gln Arg Lys Ser Lys Pro  
 340 345 350  
 Asn Met Asn Tyr Asp Lys Leu Ser Arg Ala Leu Arg Tyr Tyr Tyr Asp  
 355 360 365  
 Lys Asn Ile Met Thr Lys Val His Gly Lys Arg Tyr Ala Tyr Lys Phe  
 370 375 380  
 Asp Phe His Gly Ile Ala Gln Ala Leu Gln Pro His Pro Thr Glu Ser  
 385 390 395 400  
 Ser Met Tyr Lys Tyr Pro Ser Asp Ile Ser Tyr Met Pro Ser Tyr His  
 405 410 415  
 Ala His Gln Gln Lys Val Asn Phe Val Pro Pro His Pro Ser Ser Met  
 420 425 430  
 Pro Val Thr Ser Ser Ser Phe Phe Gly Ala Ala Ser Gln Tyr Trp Thr  
 435 440 445  
 Ser Pro Thr Gly Gly Ile Tyr Pro Asn Pro Asn Val Pro Arg His Pro  
 450 455 460  
 Asn Thr His Val Pro Ser His Leu Gly Ser Tyr Tyr  
 465 470 475

&lt;210&gt; 147

&lt;211&gt; 1431

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 147

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atggcggtcca cggattacag tacctatagc caagctgcag cgcagcaggg ctacagtgct 60
tacaccgccc agcccactca aggatatgca cagaccaccc aggcataatgg gcaacaaagc 120
tatggaacct atggacagcc cactgatgtc agctataccc aggctcagac cactgcaacc 180
tatgggcaga ccgcctatgc aacttcttat ggacagcctc ccactgggta tactactcca 240
actgcccccc aggcatacag ccagcctgtc caggggtatg gcactgggtgc ttatgatacc 300
accactgcta cagtcaccac caccagggcc tcctatgcag ctacagtctgc atatggcact 360
cagcctgctt atccagccta tgggcagcag ccagcagcca ctgcacctac aagaccgcag 420
gatggaaaca agcccactga gactagtcaa cctcaatcta gcacaggggg ttacaaccag 480
cccagcctag gatattggaca gagtaactac agttatcccc aggtacctgg gagctacccc 540
atgcagccag tcaactgcac tccatcctac cctcctacca gctattcctc tacacagccg 600
actagttatg atcagagcag ttactctcag cagaacacct atgggcaacc gagcagctat 660
ggacagcaga gtagctatgg tcaacaaagc agctatgggc agcagcctcc cactagttac 720
ccaccccaaa ctggatccta cagccaagct ccaagtcaat atagccaaca gagcagcagc 780
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tccatgtaca agtacccttc tgacatctcc tacatgcctt cctaccatgc ccaccagcag 1260
aaggtgaact ttgtccctcc ccatccatcg tccatgcctg tcacttcctc cagcttcttt 1320
ggagccgcat cacaatactg gacctcccc acggggggaa tctaccccaa ccccaacgtc 1380
ccccgccatc ctaacaccca cgtgccttca cacttaggca gctactacta g 1431

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117/299

<210> 148  
 <211> 154  
 <212> PRT  
 <213> Homo sapiens

<400> 148  
 Met Asp Leu Pro Tyr Tyr His Gly Arg Leu Thr Lys Gln Asp Cys Glu  
           1                  5                  10                  15  
 Thr Leu Leu Leu Lys Glu Gly Val Asp Gly Asn Phe Leu Leu Arg Asp  
                   20                  25                  30  
 Ser Glu Ser Ile Pro Gly Val Leu Cys Leu Cys Val Ser Phe Lys Asn  
                   35                  40                  45  
 Ile Val Tyr Thr Tyr Arg Ile Phe Arg Glu Lys His Gly Tyr Tyr Arg  
           50                  55                  60  
 Ile Gln Pro Ile Lys Arg Thr Ser Pro Ser Leu Arg Trp Arg Gly Ser  
           65                  70                  75                  80  
 Lys Leu Glu Leu Glu Ala Phe Met Thr Ala Glu Gly Ser Pro Lys Gln  
                   85                  90                  95  
 Val Phe Pro Ser Leu Lys Glu Leu Ile Ser Lys Phe Glu Lys Pro Asn  
                   100                  105                  110  
 Gln Gly Met Val Val His Leu Leu Lys Pro Ile Lys Arg Thr Ser Pro  
           115                  120                  125  
 Ser Leu Arg Trp Arg Gly Leu Lys Leu Glu Leu Glu Thr Phe Val Asn  
           130                  135                  140  
 Ser Asn Ser Asp Tyr Val Asp Val Leu Pro  
           145                  150

<210> 149  
 <211> 465  
 <212> DNA  
 <213> Homo sapiens

<400> 149  
 atggatctgc cttactacca tggacgtctg accaagcaag actgtgagac cttgctgctc 60  
 aaggaagggg tggatggcaa ctttctttta agagacagcg agtcgatacc aggagtccctg 120  
 tgcctctgtg tctcgtttaa aaatattgtc tacacatacc gaatcttcag agagaaacac 180  
 ggggtattaca ggatacagcc aataaagaga accagcccca gcttgagatg gagaggatcg 240  
 aaattagagt tggaagcatt tatgactgca gaaggttctc caaaacaggt ctttccaagc 300  
 ctaaaggaac tgatctccaa atttgaaaaa ccaaatacagg ggatgggtggg tcacctttta 360  
 aagccaataa agagaaccag cccagcttg agatggagag gattgaaatt agagttggaa 420  
 acatttgtga acagtaacag cgattatgtg gatgtcttgc cttga 465

<210> 150  
 <211> 132  
 <212> PRT

118/299

&lt;213&gt; Homo sapiens

&lt;400&gt; 150

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Met Asp Leu Pro Tyr Tyr His Gly Arg Leu Thr Lys Gln Asp Cys Glu
 1             5             10             15

Thr Leu Leu Leu Lys Glu Gly Val Asp Gly Asn Phe Leu Leu Arg Asp
          20             25             30

Ser Glu Ser Ile Pro Gly Val Leu Cys Leu Cys Val Ser Phe Lys Asn
          35             40             45

Ile Val Tyr Thr Tyr Arg Ile Phe Arg Glu Lys His Gly Tyr Tyr Arg
          50             55             60

Ile Gln Thr Ala Glu Gly Ser Pro Lys Gln Val Phe Pro Ser Leu Lys
          65             70             75             80

Glu Leu Ile Ser Lys Phe Glu Lys Pro Asn Gln Gly Met Val Val His
          85             90             95

Leu Leu Lys Pro Ile Lys Arg Thr Ser Pro Ser Leu Arg Trp Arg Gly
          100            105            110

Leu Lys Leu Glu Leu Glu Thr Phe Val Asn Ser Asn Ser Asp Tyr Val
          115            120            125

Asp Val Leu Pro
          130

```

&lt;210&gt; 151

&lt;211&gt; 420

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 151

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atggatctgc cttactacca tggacgtctg accaagcaag actgtgagac cttgctgctc 60
aaggaagggg tggatggcaa ctttctttta agagacagcg agtcgatacc aggagtcctg 120
tgcctctgtg tctcgtttaa aaatattgtc tacacatacc gaatcttcag agagaaacac 180
gggtattaca ggatacagac tgcagaaggt tctccaaaac aggtctttcc aagcctaaag 240
gaactgatct ccaaatttga aaaaccaa at caggggatgg tggttcacct tttaaagcca 300
ataaagagaa ccagccccag cttgagatgg agaggattga aattagagtt ggaaacattt 360
gtgaacagta acagcgatta tgtggatgtc ttgccttgaa gataaggctg cggacaaaag 420

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&lt;210&gt; 152

&lt;211&gt; 45

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 152

```

Met Asp Leu Pro Tyr Tyr His Gly Arg Leu Thr Lys Gln Asp Cys Glu
 1             5             10             15

Thr Leu Leu Leu Lys Glu Gly Val Asp Gly Asn Phe Leu Leu Arg Asp
          20             25             30

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119/299

Ser Glu Ser Ile Pro Gly Val Leu Cys Leu Cys Val Ser  
           35                          40                          45

<210> 153  
 <211> 136  
 <212> DNA  
 <213> Homo sapiens

<400> 153  
 atggatctgc cttactacca tggacgtctg accaagcaag actgtgagac cttgctgctc 60  
 aaggaagggg tggatggcaa ctttctttta agagacagcg agtcgatacc aggagtcctg 120  
 tgcctctgtg tctcgt  136

<210> 154  
 <211> 132  
 <212> PRT  
 <213> Mus musculus

<400> 154  
 Met Asp Leu Pro Tyr Tyr His Gly Cys Leu Thr Lys Arg Glu Cys Glu  
   1                          5                          10                          15  
 Ala Leu Leu Leu Lys Gly Gly Val Asp Gly Asn Phe Leu Ile Arg Asp  
                           20                          25                          30  
 Ser Glu Ser Val Pro Gly Ala Leu Cys Leu Cys Val Ser Phe Lys Lys  
           35                          40                          45  
 Leu Val Tyr Ser Tyr Arg Ile Phe Arg Glu Lys His Gly Tyr Tyr Arg  
   50                          55                          60  
 Ile Glu Thr Asp Ala His Thr Pro Arg Thr Ile Phe Pro Asn Leu Gln  
   65                          70                          75                          80  
 Glu Leu Val Ser Lys Tyr Gly Lys Pro Gly Gln Gly Leu Val Val His  
                           85                          90                          95  
 Leu Ser Asn Pro Ile Met Arg Asn Asn Leu Cys Gln Arg Gly Arg Arg  
           100                          105                          110  
 Met Glu Leu Glu Leu Asn Val Tyr Glu Asn Thr Asp Glu Glu Tyr Val  
           115                          120                          125  
 Asp Val Leu Pro  
           130

<210> 155  
 <211> 399  
 <212> DNA  
 <213> Mus musculus

<400> 155  
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 aagggaggtg tggatggcaa ctttctgata agagacagcg agtctgtgcc aggagccctg 120  
 tgcctctgtg tctcgtttta aaagcttgtc tacagctacc gaatcttcag agagaaacat 180

120/299

```

ggatattaca ggatagagac tgatgctcat actccaagaa cgatctttcc aaacctacag 240
gaattggtct ccaaatatgg aaaaccgggt caaggattgg tggttcacct ttcaaaccga 300
ataatgagaa acaacctatg ccaaagaggg agaagaatgg agttagagct gaatgtttat 360
gagaacactg atgaggagta tgtggacgtc ttgccttga 399

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<210> 156  
 <211> 76  
 <212> PRT  
 <213> Homo sapiens

<400> 156  
 Pro Thr Ser Tyr Pro Pro Gln Thr Gly Ser Tyr Ser Gln Ala Pro Ser  
 1 5 10 15  
 Gln Tyr Ser Gln Gln Ser Ser Ser Tyr Gly Gln Gln Asn Pro Tyr Gln  
 20 25 30  
 Ile Leu Gly Pro Thr Ser Ser Arg Leu Ala Asn Pro Gly Ser Gly Gln  
 35 40 45  
 Ile Gln Leu Trp Gln Phe Leu Leu Glu Leu Leu Ser Asp Ser Ala Asn  
 50 55 60  
 Ala Ser Cys Ile Thr Trp Glu Gly Thr Asn Gly Glu  
 65 70 75

<210> 157  
 <211> 229  
 <212> DNA  
 <213> Homo sapiens

<400> 157  
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 cagagcagca gctacgggca gcagaatccg tatcagatcc tgggcccgcag cagcagtcgc 120  
 ctagccaacc ctggaagcgg gcagatccag ctgtggcaat tcctcctgga gctgctctcc 180  
 gacagcgcca acgccagctg tatcacctgg gaggggacca acggggagt 229

<210> 158  
 <211> 100  
 <212> DNA  
 <213> Homo sapiens

<400> 158  
 tacgggcagc agagttcact gctggcctat aatacaacct cccacaccga ccaatcctca 60  
 cgattgagtg tcaaagaaga cccttcttat gactcagtca 100

<210> 159  
 <211> 20  
 <212> PRT  
 <213> Homo sapiens

<400> 159  
 Ser Gln Gln Ser Ser Ser Tyr Gly Gln Gln Ser Pro Pro Leu Gly Gly  
 1 5 10 15

121/299

Ala Gln Thr Ile  
20

<210> 160  
<211> 60  
<212> DNA  
<213> Homo sapiens

<400> 160  
agccaacaga gcagcagcta cgggcagcag agtcctcccc ttggaggggc acaaacgata 60

<210> 161  
<211> 447  
<212> DNA  
<213> Homo sapiens

<400> 161  
agatagagct ggagacctac aaactgaagt gcaaggcact gcaggaggag aaccgcgacc 60  
tgcgcaaagc cagcgttacc atcatactgg agaacaggcc atctgttctg tttctacctg 120  
tcccctggag gctgcccaga aaccggccct cgctggactc catggagAAC cagggtctccg 180  
tggatgcctt caagatcctg gaggatccaa agtgggaatt ccctcggaag aacttggttc 240  
ttggaaaaac tctaggagaa ggcgaatttg gaaaagtggc caaggcaacg gccttccatc 300  
tgaaaggcag agcagggtac accacggtgg ccgtgaagat gctgaaagag aacgcctccc 360  
cgagtgaagt tgcagacctg ctgtcagagt tcaacgtcct gaagcaggtc aaccacccac 420  
atgtcatcaa attgtatggg gcctgca 447

<210> 162  
<211> 585  
<212> PRT  
<213> Homo sapiens

<400> 162  
Met Ala Asp Ser Ala Ser Glu Ser Asp Thr Asp Gly Ala Gly Gly Asn  
1 5 10 15  
Ser Ser Ser Ser Ala Ala Met Gln Ser Ser Cys Ser Ser Thr Ser Gly  
20 25 30  
Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Lys Ser Gly Gly  
35 40 45  
Ile Val Ile Ser Pro Phe Arg Leu Glu Glu Leu Thr Asn Arg Leu Ala  
50 55 60  
Ser Leu Gln Gln Glu Asn Lys Val Leu Lys Ile Glu Leu Glu Thr Tyr  
65 70 75 80  
Lys Leu Lys Cys Lys Ala Leu Gln Glu Glu Asn Arg Asp Leu Arg Lys  
85 90 95  
Ala Ser Val Thr Ile Gln Ala Arg Ala Glu Gln Glu Glu Glu Phe Ile  
100 105 110  
Ser Asn Thr Leu Phe Lys Lys Ile Gln Ala Leu Gln Lys Glu Lys Glu



122/299

115					120					125					
Thr	Leu	Ala	Val	Asn	Tyr	Glu	Lys	Glu	Glu	Glu	Phe	Leu	Thr	Asn	Glu
130						135					140				
Leu	Ser	Arg	Lys	Leu	Met	Gln	Leu	Gln	His	Glu	Lys	Gly	Glu	Leu	Glu
145					150					155					160
Gln	His	Leu	Glu	Gln	Glu	Gln	Glu	Phe	Gln	Val	Asn	Lys	Leu	Met	Lys
				165					170					175	
Lys	Ile	Lys	Lys	Leu	Glu	Asn	Asp	Thr	Ile	Ser	Lys	Gln	Leu	Thr	Leu
			180					185					190		
Glu	Gln	Leu	Arg	Arg	Glu	Lys	Ile	Asp	Leu	Glu	Asn	Thr	Leu	Glu	Gln
		195					200					205			
Glu	Gln	Glu	Ala	Leu	Val	Asn	Arg	Leu	Trp	Lys	Arg	Met	Asp	Lys	Leu
		210				215					220				
Glu	Ala	Glu	Thr	Arg	Ile	Leu	Gln	Glu	Lys	Leu	Asp	Gln	Pro	Val	Ser
225					230					235					240
Ala	Pro	Pro	Ser	Pro	Arg	Asp	Ile	Ser	Met	Glu	Ile	Asp	Ser	Pro	Glu
				245					250					255	
Asn	Met	Met	Arg	His	Ile	Arg	Phe	Leu	Lys	Asn	Glu	Val	Glu	Arg	Leu
			260					265					270		
Lys	Lys	Gln	Leu	Arg	Ala	Ala	Gln	Leu	Gln	His	Ser	Glu	Lys	Met	Ala
		275					280					285			
Gln	Tyr	Leu	Glu	Glu	Glu	Arg	His	Met	Arg	Glu	Glu	Asn	Leu	Arg	Leu
	290					295						300			
Gln	Arg	Lys	Leu	Gln	Arg	Glu	Met	Glu	Arg	Arg	Glu	Ala	Leu	Cys	Arg
305					310					315					320
Gln	Leu	Ser	Glu	Ser	Glu	Ser	Ser	Leu	Glu	Met	Asp	Asp	Glu	Arg	Tyr
				325					330					335	
Phe	Asn	Glu	Met	Ser	Ala	Gln	Gly	Leu	Arg	Pro	Arg	Thr	Val	Ser	Ser
			340					345					350		
Pro	Ile	Pro	Tyr	Thr	Pro	Ser	Pro	Ser	Ser	Ser	Arg	Pro	Ile	Ser	Pro
		355					360					365			
Gly	Leu	Ser	Tyr	Ala	Ser	His	Thr	Val	Gly	Phe	Thr	Pro	Pro	Thr	Ser
	370					375					380				
Leu	Thr	Arg	Ala	Gly	Met	Ser	Tyr	Tyr	Asn	Ser	Pro	Gly	Leu	His	Val
385					390					395					400
Gln	His	Met	Gly	Thr	Ser	His	Gly	Ile	Thr	Arg	Pro	Ser	Pro	Arg	Arg
				405					410					415	
Ser	Asn	Ser	Pro	Asp	Lys	Phe	Lys	Arg	Pro	Thr	Pro	Pro	Pro	Ser	Pro
			420					425						430	

123/299

Asn Thr Gln Thr Pro Val Gln Pro Pro Pro Pro Pro Pro Pro Pro Pro  
435 440 445

Met Gln Pro Thr Val Pro Ser Gly Ser His Leu Ala Ala Tyr Ser Phe  
450 455 460

Ala Thr Phe Gly Ala His Leu Leu Pro Ala Leu Met His Glu Leu Ser  
465 470 475 480

Leu Asn Phe Lys Leu Gly Leu Ile Gln Trp Ser Arg Leu Leu Asn Ala  
485 490 495

Lys Gly Ser Phe Ser Gly Ile Phe Gly Tyr Asp Leu Phe Ala Leu Arg  
500 505 510

Leu Ser Arg Leu His Tyr Pro Leu Cys Cys Lys Cys Leu Ser Glu Met  
515 520 525

Gln Pro Val Leu Trp Val Tyr Asn Thr Asn Gln Thr Thr Phe Ser Ile  
530 535 540

Ser Val Leu Leu Glu Ser Ser Cys Thr Ser Ile Pro Trp Leu Glu Pro  
545 550 555 560

Ser Leu Phe Gly Ile Trp Tyr Phe Ser Ser Ser Val Gln Phe Leu Leu  
565 570 575

Gly Pro Glu Leu His Ser Pro Gly Phe  
580 585

&lt;210&gt; 163

&lt;211&gt; 3011

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 163

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tcgacctcgg gcggcgggcg tggcgggcgg ggaggcgggc gcggtgggaa gtcggggggc 180
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124/299

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aaaaaaaaa a 3011

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&lt;210&gt; 164

&lt;211&gt; 447

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 164

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accagacggc ggcgggcggg tcccggagct ttcagccagc tttgctgggc ggcctaggga 180
gcgcgcccag cccggctgga gcgagcccca gtgcaatact gcccagccc gggcggggtc 240
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ccgctccgag tctgcgccct ggtgccaggg gctcagctcg gcgctcccct gtgctcgccc 360
ggcgcccact cattcgagc ccggccttcg tcgcgcgcgc ctccctgctg ctccctctcc 420
tttccccagc ccgcccggc catggcg 447

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&lt;210&gt; 165

&lt;211&gt; 585

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 165

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Met Ala Asp Ser Ala Ser Glu Ser Asp Thr Asp Gly Ala Gly Gly Asn
1           5           10          15

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125/299

Ser Ser Ser Ser Ala Ala Met Gln Ser Ser Cys Ser Ser Thr Ser Gly  
                   20                                  25                                  30

Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Lys Ser Gly Gly  
                   35                                  40                                  45

Ile Val Ile Ser Pro Phe Arg Leu Glu Glu Leu Thr Asn Arg Leu Ala  
                   50                                  55                                  60

Ser Leu Gln Gln Glu Asn Lys Val Leu Lys Ile Glu Leu Glu Thr Tyr  
                   65                                  70                                  75                                  80

Lys Leu Lys Cys Lys Ala Leu Gln Glu Glu Asn Arg Asp Leu Arg Lys  
                                   85                                  90                                  95

Ala Ser Val Thr Ile Gln Ala Arg Ala Glu Gln Glu Glu Glu Phe Ile  
                                   100                                  105                                  110

Ser Asn Thr Leu Phe Lys Lys Ile Gln Ala Leu Gln Lys Glu Lys Glu  
                   115                                  120                                  125

Thr Leu Ala Val Asn Tyr Glu Lys Glu Glu Glu Phe Leu Thr Asn Glu  
                   130                                  135                                  140

Leu Ser Arg Lys Leu Met Gln Leu Gln His Glu Lys Gly Glu Leu Glu  
 145                                  150                                  155                                  160

Gln His Leu Glu Gln Glu Gln Glu Phe Gln Val Asn Lys Leu Met Lys  
                                   165                                  170                                  175

Lys Ile Lys Lys Leu Glu Asn Asp Thr Ile Ser Lys Gln Leu Thr Leu  
                   180                                  185                                  190

Glu Gln Leu Arg Arg Glu Lys Ile Asp Leu Glu Asn Thr Leu Glu Gln  
                   195                                  200                                  205

Glu Gln Glu Ala Leu Val Asn Arg Leu Trp Lys Arg Met Asp Lys Leu  
                   210                                  215                                  220

Glu Ala Glu Thr Arg Ile Leu Gln Glu Lys Leu Asp Gln Pro Val Ser  
 225                                  230                                  235                                  240

Ala Pro Pro Ser Pro Arg Asp Ile Ser Met Glu Ile Asp Ser Pro Glu  
                                   245                                  250                                  255

Asn Met Met Arg His Ile Arg Phe Leu Lys Asn Glu Val Glu Arg Leu  
                   260                                  265                                  270

Lys Lys Gln Leu Arg Ala Ala Gln Leu Gln His Ser Glu Lys Met Ala  
                   275                                  280                                  285

Gln Tyr Leu Glu Glu Glu Arg His Met Arg Glu Glu Asn Leu Arg Leu  
                   290                                  295                                  300

Gln Arg Lys Leu Gln Arg Glu Met Glu Arg Arg Glu Ala Leu Cys Arg  
 305                                  310                                  315                                  320

Gln Leu Ser Glu Ser Glu Ser Ser Leu Glu Met Asp Asp Glu Arg Tyr

126/299

325								330				335			
Phe	Asn	Glu	Met	Ser	Ala	Gln	Gly	Leu	Arg	Pro	Arg	Thr	Val	Ser	Ser
			340								345			350	
Pro	Ile	Pro	Tyr	Thr	Pro	Ser	Pro	Ser	Ser	Ser	Arg	Pro	Ile	Ser	Pro
		355					360					365			
Gly	Leu	Ser	Tyr	Ala	Ser	His	Thr	Val	Gly	Phe	Thr	Pro	Pro	Thr	Ser
	370					375					380				
Leu	Thr	Arg	Ala	Gly	Met	Ser	Tyr	Tyr	Asn	Ser	Pro	Gly	Leu	His	Val
385					390				395						400
Gln	His	Met	Gly	Thr	Ser	His	Gly	Ile	Thr	Arg	Pro	Ser	Pro	Arg	Arg
			405						410					415	
Ser	Asn	Ser	Pro	Asp	Lys	Phe	Lys	Arg	Pro	Thr	Pro	Pro	Pro	Ser	Pro
			420						425				430		
Asn	Thr	Gln	Thr	Pro	Val	Gln	Pro	Pro	Pro	Pro	Pro	Pro	Pro	Pro	Pro
		435					440					445			
Met	Gln	Pro	Thr	Val	Pro	Ser	Gly	Ser	His	Leu	Ala	Ala	Tyr	Ser	Phe
	450					455					460				
Ala	Thr	Phe	Gly	Ala	His	Leu	Leu	Pro	Ala	Leu	Met	His	Glu	Leu	Ser
465					470					475					480
Leu	Asn	Phe	Lys	Leu	Gly	Leu	Ile	Gln	Trp	Ser	Arg	Leu	Leu	Asn	Ala
			485						490					495	
Lys	Gly	Ser	Phe	Ser	Gly	Ile	Phe	Gly	Tyr	Asp	Leu	Phe	Ala	Leu	Arg
			500						505				510		
Leu	Ser	Arg	Leu	His	Tyr	Pro	Leu	Cys	Cys	Lys	Cys	Leu	Ser	Glu	Met
		515					520					525			
Gln	Pro	Val	Leu	Trp	Val	Tyr	Asn	Thr	Asn	Gln	Thr	Thr	Phe	Ser	Ile
	530					535					540				
Ser	Val	Leu	Leu	Glu	Ser	Ser	Cys	Thr	Ser	Ile	Pro	Trp	Leu	Glu	Pro
545					550					555					560
Ser	Leu	Phe	Gly	Ile	Trp	Tyr	Phe	Ser	Ser	Ser	Val	Gln	Phe	Leu	Leu
			565						570					575	
Gly	Pro	Glu	Leu	His	Ser	Pro	Gly	Phe							
			580					585							

&lt;210&gt; 166

&lt;211&gt; 3011

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 166

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127/299

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&lt;210&gt; 167

&lt;211&gt; 808

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 167

128/299

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&lt;210&gt; 168

&lt;211&gt; 271

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 168

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Met Glu Asp Ser His Lys Ser Thr Thr Ser Glu Thr Ala Pro Gln Pro
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Gly Ser Ala Val Gln Gly Ala His Ile Ser His Ile Ala Gln Gln Val
                20                      25                      30

Ser Ser Leu Ser Glu Ser Glu Glu Ser Gln Asp Ser Ser Asp Ser Ile
  35                      40                      45

Gly Ser Ser Gln Lys Ala His Gly Ile Leu Ala Arg Arg Pro Ser Tyr
  50                      55                      60

Arg Lys Ile Leu Lys Asp Leu Ser Ser Glu Asp Thr Arg Gly Arg Lys
  65                      70                      75                      80

Gly Asp Gly Glu Asn Ser Gly Val Ser Ala Ala Val Thr Ser Met Ser
                85                      90                      95

Val Pro Thr Pro Ile Tyr Gln Thr Ser Ser Gly Gln Tyr Ile Ala Ile
  100                      105                      110

Ala Pro Asn Gly Ala Leu Gln Leu Ala Ser Pro Gly Thr Asp Gly Val
  115                      120                      125

Gln Gly Leu Gln Thr Leu Thr Met Thr Asn Ser Gly Ser Thr Gln Gln
  130                      135                      140

Gly Thr Thr Ile Leu Gln Tyr Ala Gln Thr Ser Asp Gly Gln Gln Ile
  145                      150                      155                      160

Leu Val Pro Ser Asn Gln Val Val Val Gln Thr Ala Ser Gly Asp Met
                165                      170                      175

Gln Thr Tyr Gln Ile Arg Thr Thr Pro Ser Ala Thr Ser Leu Pro Gln
  180                      185                      190

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129/299

Thr Val Val Met Thr Ser Pro Val Thr Leu Thr Ser Gln Thr Thr Lys  
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Thr Asp Asp Pro Gln Leu Lys Arg Glu Ile Arg Leu Met Lys Asn Arg  
 210 215 220

Glu Ala Ala Arg Glu Cys Arg Arg Lys Lys Lys Glu Tyr Val Lys Cys  
 225 230 235 240

Leu Glu Asn Arg Val Ala Val Leu Glu Asn Gln Asn Lys Thr Leu Ile  
 245 250 255

Glu Glu Leu Lys Thr Leu Lys Asp Leu Tyr Ser Asn Lys Ser Val  
 260 265 270

<210> 169  
 <211> 816  
 <212> DNA  
 <213> Homo sapiens

<400> 169  
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 cagggagctc acatttctca tattgctcaa caggtatcat ctttatcaga aagtgaggag 120  
 tcccaggact catccgacag cataggctcc tcacagaaag cccacgggat cctagcacgg 180  
 cgcccatctt acagaaaaat tttgaaagac ttatcttctg aagatacacg gggcagaaaa 240  
 ggagacggag aaaattcttg agtttctgct gctgtcactt ctatgtctgt tccaactccc 300  
 atctatcaga ctagcagcgg acagtacatt gccattgccc caaatggagc cttacagttg 360  
 gcaagtccag gcacagatgg agtacaggga cttcagacat taaccatgac aaattcaggc 420  
 agtactcagc aagggtacaac tattcttcag tatgcacaga cctctgatgg acagcagata 480  
 cttgtgccca gcaatcaggt ggtcgtacaa actgcatcag gagatatgca aacatatcag 540  
 atccgaacta caccttcagc tacttctctg ccacaaaactg tggatgatgac atctcctgtg 600  
 actctcacct ctgagacaac taagacagat gacccccaat tgaaaagaga aataagggtta 660  
 atgaaaaaca gagaagctgc tcgagaatgt cgcagaaaga agaaagaata tgtgaaatgc 720  
 ctggaaaacc gagttgcagt cctggaaaat caaaataaaa ctctaataga agagttaaaa 780  
 actttgaagg atctttattc caataaaagt gtttga 816

<210> 170  
 <211> 117  
 <212> PRT  
 <213> Homo sapiens

<400> 170  
 Thr Gly Ser Tyr Ser Gln Ala Pro Ser Gln Tyr Ser Gln Gln Ser Ser  
 1 5 10 15

Ser Tyr Gly Gln Gln Ile Ala Ile Ala Pro Asn Gly Ala Leu Gln Leu  
 20 25 30

Ala Ser Pro Gly Thr Asp Gly Val Gln Gly Leu Gln Thr Leu Thr Met  
 35 40 45

Thr Asn Ser Gly Ser Thr Gln Gln Gly Thr Thr Ile Leu Gln Tyr Ala  
 50 55 60

Gln Thr Ser Asp Gly Gln Gln Ile Leu Val Pro Ser Asn Gln Val Val  
 65 70 75 80



130/299

Val Gln Thr Ala Ser Gly Asp Met Pro Thr Tyr Gln Ile Arg Thr Thr  
                                     85                                    90                                    95

Pro Ser Ala Thr Ser Leu Pro Gln Thr Val Val Met Thr Ser Pro Val  
                                     100                                    105                                    110

Thr Leu Thr Ser Gln  
                                     115

<210> 171  
 <211> 353  
 <212> DNA  
 <213> Homo sapiens

<400> 171  
 aactggatcc tacagccaag ctccaagtca atatagccaa cagagcagca gctacgggca 60  
 gcagattgcc attgccccaa atggagcctt acagttggca agtccaggca cagatggagt 120  
 acagggactt cagacattaa ccatgacaaa ttcaggcagt actcagcaag gtacaactat 180  
 tcttcagtat gcacagacct ctgatggaca gcagatactt gtgccagca atcagggtgg 240  
 cgtacaaact gcatacaggag atatgccaac atatcagatc cgaactacac cttcagctac 300  
 ttctctgcca caaactgtgg tgatgacatc tcctgtgact ctcacctctc aga 353

<210> 172  
 <211> 500  
 <212> DNA  
 <213> Homo sapiens

<400> 172  
 taagtgccac ggagaaagct aaagcagaga aaggaatgga gaatgttcag gatggagggtc 60  
 agagtgttac atcagggtggc caggaattac cttaggtaat tcctccactc caaaccttc 120  
 agtgacttcc atgacatgaa ataggaagtc attggagggt ttgagcagag gaatgacctg 180  
 ttttaaaagg ctactcagg ctgctgtatg gtgaatagag ttgccaacag aggccatagg 240  
 ataacagggt tttgttgaga aagtggtttc attttgaggg ctaggtggaa agacctgagg 300  
 ttgtaaccag tagtggagag ggaaggaaaa ttaactcagg gggagtgaat ctgtagacct 360  
 acttgagata agatactcgc tgggttaggt aggaggggca gataggatat ctaggcttgg 420  
 agaggctggc aactcaaata taatggatac ttaatttttt tttttttttt tgcaggggtg 480  
 agcacagaca ggatcgcagg 500

<210> 173  
 <211> 521  
 <212> DNA  
 <213> Homo sapiens

<400> 173  
 cccctaaacc agatggccca ggagggggac caggtggctc tcacatgggt aagaaaggca 60  
 gacctggtgc tagggagctg ggaccaaaga atccttaatt tttcagcggg gaggctcggg 120  
 gaacataggg gaatgggaat atgatagatc ttgtttcttt tgtcctaggg ggtaactacg 180  
 gggatgatcg tcgtgggtggc agaggaggct atgatcgagg cggctaccgg ggccgcggcg 240  
 gggaccgtgg aggccttcga gggggccggg gtggtgggga cagagggtggc tttggccctg 300  
 gcaagatgga ttccagacct tctgcagtca gaaagtttct gcagtaattt agagatggta 360  
 gtgaattgat ctagattgga aacaatggaa ttagaagtgt ttagattctt ctaagcaaag 420  
 gtttttaaaaa ctcattttta aagaatgagt taagggccgg gcattggtggc tcacacctgt 480  
 aatcccagca ctttgggaga ccagagggtg gtggatcacc t 521

131/299

&lt;210&gt; 174

&lt;211&gt; 75

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 174

Tyr Ser Gln Gln Ser Ser Gln Pro Tyr Gly Gln Gln Ser Tyr Ser Gly  
 1 5 10 15

Tyr Ser Gln Ser Thr Asp Thr Ser Gly Tyr Gly Gln Ser Ser Tyr Ser  
 20 25 30

Ser Tyr Gly Gln Ser Gln Asn Met Phe Lys Lys Glu Val Tyr Leu His  
 35 40 45

Thr Ser Pro His Leu Lys Ala Asp Val Leu Phe Gln Thr Asp Pro Thr  
 50 55 60

Ala Glu Met Ala Ala Glu Ser Leu Pro Phe Ser  
 65 70 75

&lt;210&gt; 175

&lt;211&gt; 225

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 175

tattcccagc agagcagtc gccctacgga cagcagaggtt acagtgggta tagccagtcc 60  
 acggacactt caggctatgg ccagagcagc tattcttctt atggccagag ccagaacatg 120  
 ttcaagaagg aagtgtatct tcatacatca ccacacctga aagcagatgt gcttttccag 180  
 actgatccaa ctgcagagat ggcagctgag tcattgcctt tctcc 225

&lt;210&gt; 176

&lt;211&gt; 78

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 176

Gly Asp Trp Lys Cys Pro Asn Pro Thr Cys Glu Asn Met Asn Phe Ser  
 1 5 10 15

Trp Arg Asn Glu Cys Asn Gln Cys Lys Ala Pro Lys Pro Asp Gly Pro  
 20 25 30

Gly Gly Gly Pro Gly Gly Ser His Met Gly Val Phe Lys Lys Glu Val  
 35 40 45

Tyr Leu His Thr Ser Pro His Leu Lys Ala Asp Val Leu Phe Gln Thr  
 50 55 60

Asp Pro Thr Ala Glu Met Ala Ala Glu Ser Leu Pro Phe Ser  
 65 70 75

&lt;210&gt; 177

132/299

&lt;211&gt; 235

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 177

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tggtgactgg aagtgtccta atccacacctg tgagaatatg aactttctctt ggaggaatga 60
atgcaaccag tgtaaggccc ctaaaccaga tggcccagga gggggaccag gtggctctca 120
catgggggtg ttcaagaagg aagtgtatct tcatacatca ccacacctga aagcagatgt 180
gcttttccag actgatccaa ctgcagagat ggcagctgag tcattgcctt tctcc      235

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&lt;210&gt; 178

&lt;211&gt; 526

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 178

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Met Ala Ser Asn Asp Tyr Thr Gln Gln Ala Thr Gln Ser Tyr Gly Ala
  1              5              10              15

Tyr Pro Thr Gln Pro Gly Gln Gly Tyr Ser Gln Gln Ser Ser Gln Pro
          20              25              30

Tyr Gly Gln Gln Ser Tyr Ser Gly Tyr Ser Gln Ser Thr Asp Thr Ser
          35              40              45

Gly Tyr Gly Gln Ser Ser Tyr Ser Ser Tyr Gly Gln Ser Gln Asn Thr
          50              55              60

Gly Tyr Gly Thr Gln Ser Thr Pro Gln Gly Tyr Gly Ser Thr Gly Gly
          65              70              75              80

Tyr Gly Ser Ser Gln Ser Ser Gln Ser Ser Tyr Gly Gln Gln Ser Ser
          85              90              95

Tyr Pro Gly Tyr Gly Gln Gln Pro Ala Pro Ser Ser Thr Ser Gly Ser
          100             105             110

Tyr Gly Ser Ser Ser Gln Ser Ser Ser Tyr Gly Gln Pro Gln Ser Gly
          115             120             125

Ser Tyr Ser Gln Gln Pro Ser Tyr Gly Gly Gln Gln Gln Ser Tyr Gly
          130             135             140

Gln Gln Gln Ser Tyr Asn Pro Pro Gln Gly Tyr Gly Gln Gln Asn Gln
          145             150             155             160

Tyr Asn Ser Ser Ser Gly Gly Gly Gly Gly Gly Gly Gly Gly Asn
          165             170             175

Tyr Gly Gln Asp Gln Ser Ser Met Ser Ser Gly Gly Gly Ser Gly Gly
          180             185             190

Gly Tyr Gly Asn Gln Asp Gln Ser Gly Gly Gly Gly Ser Gly Gly Tyr
          195             200             205

Gly Gln Gln Asp Arg Gly Gly Arg Gly Arg Gly Gly Ser Gly Gly Gly
          210             215             220

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133/299

Gly Gly Gly Gly Gly Gly Gly Tyr Asn Arg Ser Ser Gly Gly Tyr Glu  
 225 230 235 240  
 Pro Arg Gly Arg Gly Gly Gly Arg Gly Gly Arg Gly Gly Met Gly Gly  
 245 250 255  
 Ser Asp Arg Gly Gly Phe Asn Lys Phe Gly Gly Pro Arg Asp Gln Gly  
 260 265 270  
 Ser Arg His Asp Ser Glu Gln Asp Asn Ser Asp Asn Asn Thr Ile Phe  
 275 280 285  
 Val Gln Gly Leu Gly Glu Asn Val Thr Ile Glu Ser Val Ala Asp Tyr  
 290 295 300  
 Phe Lys Gln Ile Gly Ile Ile Lys Thr Asn Lys Lys Thr Gly Gln Pro  
 305 310 315 320  
 Met Ile Asn Leu Tyr Thr Asp Arg Glu Thr Gly Lys Leu Lys Gly Glu  
 325 330 335  
 Ala Thr Val Ser Phe Asp Asp Pro Pro Ser Ala Lys Ala Ala Ile Asp  
 340 345 350  
 Trp Phe Asp Gly Lys Glu Phe Ser Gly Asn Pro Ile Lys Val Ser Phe  
 355 360 365  
 Ala Thr Arg Arg Ala Asp Phe Asn Arg Gly Gly Gly Asn Gly Arg Gly  
 370 375 380  
 Gly Arg Gly Arg Gly Gly Pro Met Gly Arg Gly Gly Tyr Gly Gly Gly  
 385 390 395 400  
 Gly Ser Gly Gly Gly Gly Arg Gly Gly Phe Pro Ser Gly Gly Gly Gly  
 405 410 415  
 Gly Gly Gly Gln Gln Arg Ala Gly Asp Trp Lys Cys Pro Asn Pro Thr  
 420 425 430  
 Cys Glu Asn Met Asn Phe Ser Trp Arg Asn Glu Cys Asn Gln Cys Lys  
 435 440 445  
 Ala Pro Lys Pro Asp Gly Pro Gly Gly Gly Pro Gly Gly Ser His Met  
 450 455 460  
 Gly Gly Asn Tyr Gly Asp Asp Arg Arg Gly Gly Arg Gly Gly Tyr Asp  
 465 470 475 480  
 Arg Gly Gly Tyr Arg Gly Arg Gly Gly Asp Arg Gly Gly Phe Arg Gly  
 485 490 495  
 Gly Arg Gly Gly Gly Asp Arg Gly Gly Phe Gly Pro Gly Lys Met Asp  
 500 505 510  
 Ser Arg Gly Glu His Arg Gln Asp Arg Arg Glu Arg Pro Tyr  
 515 520 525

134/299

<210> 179  
 <211> 1824  
 <212> DNA  
 <213> Homo sapiens

<400> 179  
 atgctcagtc ctccagggcgt cgggtgctcag cgggtgttggga acttcggttgc ttgcttgcct 60  
 gtgcgcgcgt gcgcggacat ggcctcaaac gattataccc aacaagcaac ccaaagctat 120  
 ggggcctacc ccaccagcc cgggcagggc tattcccagc agagcagtca gccctacgga 180  
 cagcagagtt acagtggta tagccagtcc acggacactt caggctatgg ccagagcagc 240  
 tattcttctt atggccagag ccagaacaca ggctatggaa ctcaagtcaac tcccaggga 300  
 tatggctcga ctggcggcta tggcagtagc cagagctccc aatcgtctta cgggcagcag 360  
 tcctcctacc ctggctatgg ccagcagcca gctcccagca gcacctcggg aagttacggt 420  
 agcagttctc agagcagcag ctatgggcag ccccagagtg ggagctacag ccagcagcct 480  
 agctatggtg gacagcagca aagctatgga cagcagcaaa gctataatcc ccctcagggc 540  
 tatggacagc agaaccagta caacagcagc agtggtggtg gaggtggagg tggaggtgga 600  
 ggtaactatg gccaaagatca atcctccatg agtagtggtg gtggcagtggt tggcgggttat 660  
 ggcaatcaag accagagtgg tggaggtggc agcgggtggct atggacagca ggaccgtgga 720  
 ggccgcggca ggggtggcag tgggtggcggc ggccggcggcg gcgggtggtg ttacaaccgc 780  
 agcagtgggt gctatgaacc cagaggtcgt ggaggtggcc gtggaggcag aggtggcatg 840  
 ggcggaagtg accgtggtgg cttcaataaa ttgggtggcc ctcgggacca aggatcacgt 900  
 catgactccg aacaggataa ttcagacaac aacaccatct ttgtgcaagg cctgggtgag 960  
 aatgttaciaa ttgagtctgt ggctgattac ttcaagcaga ttggtattat taagacaaac 1020  
 aagaaaacgg gacagcccat gattaatttg tacacagaca gggaaactgg caagctgaag 1080  
 ggagaggcaa cgggtctctt tgatgaccca ccttcagcta aagcagctat tgactgggtt 1140  
 gatggtaaag aattctccgg aaatcctatc aaggtctcat ttgctactcg ccgggcagac 1200  
 tttaatcggg gtggtggcaa tggctcgtgga ggccgagggc gaggaggacc catgggccgt 1260  
 ggaggctatg gaggtggtgg cagtgggtgt ggtggccgag gaggatttcc cagtggagggt 1320  
 ggtggcgggt gaggacagca gcgagctggt gactggaagt gtcctaatac cactgtgag 1380  
 aatatgaact tctcttggag gaatgaatgc aaccagtgtg agggccctaa accagatggc 1440  
 ccaggagggg gaccaggtgg ctctcacatg gggggtaact acggggatga tcgtcgtggt 1500  
 ggcagaggag gctatgatcg aggcggctac cggggccgcg gcggggaccg tggaggcttc 1560  
 cgagggggcc ggggtggtgg ggacagaggt ggctttggcc ctggcaagat ggattccagg 1620  
 ggtgagcaca gacaggatcg caggagagg ccgtattaat tagcctggct ccccagggtc 1680  
 tggaaacagt ttttgtcctg taccagtggt taccctcggt attttgtaac cttccaattc 1740  
 ctgatcacc aagggttttt tttgtgtcgg actatgtaat tgtaactata cctctgggtc 1800  
 ccattaaaag tgaccatttt agtt 1824

<210> 180  
 <211> 195  
 <212> PRT  
 <213> Homo sapiens

<400> 180  
 Gln Ser Ser Gln Ser Ser Tyr Gly Gln Gln Ser Ser Tyr Pro Gly Tyr  
 1 5 10 15  
 Gly Gln Gln Pro Ala Pro Ser Ser Thr Ser Gly Ser Tyr Gly Ser Ser  
 20 25 30  
 Ser Gln Ser Ser Tyr Gly Gln Pro Gln Ser Gly Ser Tyr Ser Gln  
 35 40 45  
 Gln Pro Ser Tyr Gly Gly Gln Gln Gln Ser Tyr Gly Gln Gln Gln Ser  
 50 55 60

135/299

Tyr Asn Pro Pro Gln Gly Tyr Gly Gln Gln Asn Gln Tyr Asn Ser Ser  
 65 70 75 80  
 Ser Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Asn Tyr Gly Gln Asp  
 85 90 95  
 Gln Ser Ser Met Ser Ser Gly Gly Gly Ser Gly Gly Gly Tyr Gly Asn  
 100 105 110  
 Gln Asp Gln Ser Gly Gly Gly Gly Ser Gly Gly Tyr Gly Gln Gln Asp  
 115 120 125  
 Arg Gly Gly Arg Gly Arg Gly Gly Ser Gly Gly Gly Gly Ala Ala Ala  
 130 135 140  
 Val Val Val Thr Thr Ala Ala Val Val Ala Met Asn Pro Glu Val Val  
 145 150 155 160  
 Glu Val Ala Val Glu Ala Glu Val Ala Trp Ala Glu Val Thr Val Val  
 165 170 175  
 Ala Ser Ile Asn Leu Val Cys Ser Arg Arg Lys Cys Ile Phe Ile His  
 180 185 190  
 His His Ser  
 195

&lt;210&gt; 181

&lt;211&gt; 652

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 181

cagagctccc aatcgtctta cgggcagcag tcctcctacc ctggctatgg ccagcagcca 60  
 gctcccagca gcacctcggg aagttacggg agcagttctc agagcagcag ctatgggcag 120  
 ccccagagtg ggagctacag ccagcagcct agctatgggtg gacagcagca aagctatgga 180  
 cagcagcaaaa gctataatcc ccctcagggc tatggacagc agaaccagta caacagcagc 240  
 agtgggtgggtg gaggtggagg tggaggtgga ggtaactatg gccaagatca atcctccatg 300  
 agtagtggtg gtggcagtgg tggcggttat ggcaatcaag accagagtgg tggaggtggc 360  
 agcgggtggct atggacagca ggaccgtgga ggccgcggca ggggtggcag tgggtggcggc 420  
 ggggcggcgg cggtgggtgt tacaaccgca gcagtgggtg ctatgaacct agaggtcgtg 480  
 gaggtggccg tggaggcaga ggtggcatgg gcggaagtga ccgtgggtggc ttcaataaat 540  
 ttggtgtgtt caagaaggaa gtgtatcttc atacatcacc actcctgaaa gcagatgtgc 600  
 ttttcagac tgatccaact gcagagatgg cagctgagtc attgccttcc tc 652

&lt;210&gt; 182

&lt;211&gt; 462

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 182

Met Ala Ser Asn Asp Tyr Thr Gln Gln Ala Thr Gln Ser Tyr Gly Ala  
 1 5 10 15  
 Tyr Pro Thr Gln Pro Gly Gln Gly Tyr Ser Gln Gln Ser Ser Gln Pro  
 20 25 30

136/299

Tyr Gly Gln Gln Ser Tyr Ser Gly Tyr Ser Gln Ser Thr Asp Thr Ser  
                   35                                  40                                  45  
 Gly Tyr Gly Gln Ser Ser Tyr Ser Ser Tyr Gly Gln Ser Gln Asn Thr  
           50                                  55                                  60  
 Gly Tyr Gly Thr Gln Ser Thr Pro Gln Gly Tyr Gly Ser Thr Gly Gly  
   65                                  70                                  75                                  80  
 Tyr Gly Ser Ser Gln Ser Ser Gln Ser Ser Tyr Gly Gln Gln Ser Ser  
                                   85                                  90                                  95  
 Tyr Pro Gly Tyr Gly Gln Gln Pro Ala Pro Ser Ser Thr Ser Gly Ser  
                   100                                  105                                  110  
 Tyr Gly Ser Ser Ser Gln Ser Ser Tyr Gly Gln Pro Gln Ser Gly  
           115                                  120                                  125  
 Ser Tyr Ser Gln Gln Pro Ser Tyr Gly Gly Gln Gln Gln Ser Tyr Gly  
   130                                  135                                  140  
 Gln Gln Gln Ser Tyr Asn Pro Pro Gln Gly Tyr Gly Gln Gln Asn Gln  
 145                                  150                                  155                                  160  
 Tyr Asn Ser Ser Ser Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Asn  
                                   165                                  170                                  175  
 Tyr Gly Gln Asp Gln Ser Ser Met Ser Ser Gly Gly Gly Ser Gly Gly  
           180                                  185                                  190  
 Gly Tyr Gly Asn Gln Asp Gln Ser Gly Gly Gly Gly Ser Gly Gly Tyr  
           195                                  200                                  205  
 Gly Gln Gln Asp Arg Gly Gly Arg Gly Arg Gly Gly Ser Gly Gly Gly  
   210                                  215                                  220  
 Gly Gly Gly Gly Gly Gly Gly Tyr Asn Arg Ser Ser Gly Gly Tyr Glu  
 225                                  230                                  235                                  240  
 Pro Arg Gly Arg Gly Gly Gly Arg Gly Gly Arg Gly Gly Met Gly Gly  
                                   245                                  250                                  255  
 Ser Asp Arg Gly Gly Phe Asn Lys Phe Gly Val Phe Lys Lys Glu Val  
           260                                  265                                  270  
 Tyr Leu His Thr Ser Pro His Leu Lys Ala Asp Val Leu Phe Gln Thr  
   275                                  280                                  285  
 Asp Pro Thr Ala Glu Met Ala Ala Glu Ser Leu Pro Phe Ser Phe Gly  
   290                                  295                                  300  
 Thr Leu Ser Ser Trp Glu Leu Glu Ala Trp Tyr Glu Asp Leu Gln Glu  
 305                                  310                                  315                                  320  
 Val Leu Ser Ser Asp Glu Asn Gly Gly Thr Tyr Val Ser Pro Pro Gly  
           325                                  330                                  335

137/299

Asn Glu Glu Glu Glu Ser Lys Ile Phe Thr Thr Leu Asp Pro Ala Ser  
                   340                                  345                                  350  
 Leu Ala Trp Leu Thr Glu Glu Glu Pro Glu Pro Ala Glu Val Thr Ser  
                   355                                  360                                  365  
 Thr Ser Gln Ser Pro His Ser Pro Asp Ser Ser Gln Ser Ser Leu Ala  
                   370                                  375                                  380  
 Gln Glu Glu Glu Glu Glu Asp Gln Gly Arg Thr Arg Lys Arg Lys Gln  
                   385                                  390                                  395                                  400  
 Ser Gly His Ser Pro Ala Arg Ala Gly Lys Gln Arg Met Lys Glu Lys  
                                   405                                  410                                  415  
 Glu Gln Glu Asn Glu Arg Lys Val Ala Gln Leu Ala Glu Glu Asn Glu  
                                   420                                  425                                  430  
 Arg Leu Lys Gln Glu Ile Glu Arg Leu Thr Arg Glu Val Glu Ala Thr  
                   435                                  440                                  445  
 Arg Arg Ala Leu Ile Asp Arg Met Val Asn Leu His Gln Ala  
                   450                                  455                                  460

&lt;210&gt; 183

&lt;211&gt; 1678

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 183

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gcggccgctg tcggtgctca gcggtgttgg aacttcgttg cttgcttgcc tgtgcgcgcg 60
tgcgcggaaca tggcctcaaa cgattatacc caacaagcaa cccaaagcta tggggcctac 120
cccaccagc ccgggcaggg ctattcccag cagagcagtc agccctacgg acagcagagt 180
tacagtgggt atagccagtc cacggacact tcaggctatg gccagagcag ctattcttct 240
tatggccaga gccagaacac aggctatgga actcagtcaa ctcccagggt atatggctcg 300
actggcgggt atggcagtag ccagagctcc caatcgtctt acgggcagca gtcctcctac 360
cctggctatg gccagcagcc agctcccagc agcacctcgg gaagttacgg tagcagttct 420
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cagaaccagt acaacagcag cagtgggtgg ggaggtggag gtggaggtgg aggtaactat 600
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aggggtggca gtggtggcgg cggcggcggc ggcggtgttg gttacaaccg cagcagtggt 780
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cggaacaga gtggtcattc cccagcccgg gctggaaagc agcgcatgaa ggagaaagaa 1320
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atcgagcgcc tgaccaggga agtagaggcg actcgccgag ctctgattga ccgaatggtg 1440
aatctgcacc aagcatgaac aattgggagc atcagtcgcc cacttgggcc acactacca 1500
cctttcccag aagtggctac tgactaccct ctcactagtg ccaatgatgt gacctcaat 1560
cccacatacg caggggggag gcttggagta gacaaaagga aaggtctcag cttgtatata 1620

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138/299

gagattgtac atttatttat tactgtccct atctattaaa gtgactttct atgaaaaa 1678

&lt;210&gt; 184

&lt;211&gt; 525

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 184

Met	Ala	Ser	Asn	Asp	Tyr	Thr	Gln	Gln	Ala	Thr	Gln	Ser	Tyr	Gly	Ala
1				5					10					15	

Tyr	Pro	Thr	Gln	Pro	Gly	Gln	Gly	Tyr	Ser	Gln	Gln	Ser	Ser	Gln	Pro
			20					25					30		

Tyr	Gly	Gln	Gln	Ser	Tyr	Ser	Gly	Tyr	Ser	Gln	Ser	Thr	Asp	Thr	Ser
		35					40					45			

Gly	Tyr	Gly	Gln	Ser	Ser	Tyr	Ser	Ser	Tyr	Gly	Gln	Ser	Gln	Asn	Ser
	50					55					60				

Tyr	Gly	Thr	Gln	Ser	Thr	Pro	Gln	Gly	Tyr	Gly	Ser	Thr	Gly	Gly	Tyr
65					70					75					80

Gly	Ser	Ser	Gln	Ser	Ser	Gln	Ser	Ser	Tyr	Gly	Gln	Gln	Ser	Ser	Tyr
			85						90					95	

Pro	Gly	Tyr	Gly	Gln	Gln	Pro	Ala	Pro	Ser	Ser	Thr	Ser	Gly	Ser	Tyr
			100					105					110		

Gly	Ser	Ser	Ser	Gln	Ser	Ser	Ser	Tyr	Gly	Gln	Pro	Gln	Ser	Gly	Ser
			115				120					125			

Tyr	Ser	Gln	Gln	Pro	Ser	Tyr	Gly	Gly	Gln	Gln	Gln	Ser	Tyr	Gly	Gln
130						135					140				

Gln	Gln	Ser	Tyr	Asn	Pro	Pro	Gln	Gly	Tyr	Gly	Gln	Gln	Asn	Gln	Tyr
145					150					155					160

Asn	Ser	Ser	Ser	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Asn	Tyr
				165					170					175	

Gly	Gln	Asp	Gln	Ser	Ser	Met	Ser	Ser	Gly	Gly	Gly	Ser	Gly	Gly	Gly
		180						185					190		

Tyr	Gly	Asn	Gln	Asp	Gln	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Tyr	Gly
		195					200					205			

Gln	Gln	Asp	Arg	Gly	Gly	Arg	Gly	Arg	Gly	Gly	Ser	Gly	Gly	Gly	Gly
		210				215						220			

Gly	Gly	Gly	Gly	Gly	Gly	Tyr	Asn	Arg	Ser	Ser	Gly	Gly	Tyr	Glu	Pro
225					230					235					240

Arg	Gly	Arg	Gly	Gly	Gly	Arg	Gly	Gly	Arg	Gly	Gly	Met	Gly	Gly	Ser
			245						250				255		

Asp	Arg	Gly	Gly	Phe	Asn	Lys	Phe	Gly	Gly	Pro	Arg	Asp	Gln	Gly	Ser
-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

139/299

260										265					270				
Arg	His	Asp	Ser	Glu	Gln	Asp	Asn	Ser	Asp	Asn	Asn	Thr	Ile	Phe	Val				
		275						280					285						
Gln	Gly	Leu	Gly	Glu	Asn	Val	Thr	Ile	Glu	Ser	Val	Ala	Asp	Tyr	Phe				
	290					295					300								
Lys	Gln	Ile	Gly	Ile	Ile	Lys	Thr	Asn	Lys	Lys	Thr	Gly	Gln	Pro	Met				
305					310					315					320				
Ile	Asn	Leu	Tyr	Thr	Asp	Arg	Glu	Thr	Gly	Lys	Leu	Lys	Gly	Glu	Ala				
				325					330					335					
Thr	Val	Ser	Phe	Asp	Asp	Pro	Pro	Ser	Ala	Lys	Ala	Ala	Ile	Asp	Trp				
			340					345					350						
Phe	Asp	Gly	Lys	Glu	Phe	Ser	Gly	Asn	Pro	Ile	Lys	Val	Ser	Phe	Ala				
		355					360					365							
Thr	Arg	Arg	Ala	Asp	Phe	Asn	Arg	Gly	Gly	Gly	Asn	Gly	Arg	Gly	Gly				
	370					375					380								
Arg	Gly	Arg	Gly	Gly	Pro	Met	Gly	Arg	Gly	Gly	Tyr	Gly	Gly	Gly	Gly				
385					390					395					400				
Ser	Gly	Gly	Gly	Gly	Arg	Gly	Gly	Phe	Pro	Ser	Gly	Gly	Gly	Gly	Gly				
				405				410						415					
Gly	Gly	Gln	Gln	Arg	Ala	Gly	Asp	Trp	Lys	Cys	Pro	Asn	Pro	Thr	Cys				
		420					425						430						
Glu	Asn	Met	Asn	Phe	Ser	Trp	Arg	Asn	Glu	Cys	Asn	Gln	Cys	Lys	Ala				
	435						440					445							
Pro	Lys	Pro	Asp	Gly	Pro	Gly	Gly	Gly	Pro	Gly	Gly	Ser	His	Met	Gly				
	450					455					460								
Gly	Asn	Tyr	Gly	Asp	Asp	Arg	Arg	Gly	Gly	Arg	Gly	Gly	Tyr	Asp	Arg				
465					470					475					480				
Gly	Gly	Tyr	Arg	Gly	Arg	Gly	Gly	Asp	Arg	Gly	Gly	Phe	Arg	Gly	Gly				
			485					490						495					
Arg	Gly	Gly	Gly	Asp	Arg	Gly	Gly	Phe	Gly	Pro	Gly	Lys	Met	Asp	Ser				
		500					505						510						
Arg	Gly	Glu	His	Arg	Gln	Asp	Arg	Arg	Glu	Arg	Pro	Tyr							
	515					520						525							

&lt;210&gt; 185

&lt;211&gt; 1822

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 185

gcggccgctg gcgtcgggtgc tcagcgggtgt tggaacttcg ttgcttgctt gcctgtgcgc 60

140/299

```

gcgtgcgcgg acatggcctc aaacgattat acccaacaag caacccaaag ctatggggcc 120
taccaccacc agcccgggca gggctattcc cagcagagca gtcagcccta cggacagcag 180
agttacagtg gttatagcca gtccacggac acttcaggct atggccagag cagctattct 240
tcttatggcc agagccagaa cagctatgga actcagtcaa ctcccagggt atatggctcg 300
actggcggct atggcagtag ccagagctcc caatcgtctt acgggcagca gtcctcctat 360
cctggctatg gccagcagcc agctcccagc agcacctcgg gaagttacgg tagcagttct 420
cagagcagca gctatgggca gccccagagt gggagctaca gccagcagcc tagctatggg 480
ggacagcagc aaagctatgg acagcagcaa agctataatc cccctcagggt ctatggacag 540
cagaaccagt acaacagcag cagtgggtgg ggaggtggag gtggaggtgg aggtaactat 600
ggccaagatc aatcctccat gagtagtggt ggtggcagtg gtggcgggta tggcaatcaa 660
gaccagagtg gtggaggtgg cagcgggtgg tatggacagc aggaccgtgg aggcgcgggc 720
aggggtggca gtgggtggcg cggcggcgcc ggcggtgggt gttacaaccg cagcagtggt 780
ggctatgaac ccagaggtcg tggaggtggc cgtggaggca gaggtggcat gggcgggaag 840
gaccgtgggt gcttcaataa atttgggtgg cctcgggacc aaggatcacg tcatgactcc 900
gaacaggata attcagacaa caacaccatc tttgtgcaag gcctgggtga gaatgttaca 960
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acgggtctct ttgatgaccc accttcagct aaagcagcta ttgactgggt tgatggtaaa 1140
gaattctccg gaaatcctat caaggtctca tttgctactc gccgggcaga ctttaatcgg 1200
ggtggtggca atggtcgtgg aggccgaggg cgaggaggac ccatgggccg tggaggctat 1260
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cgggggtggg gggacagagg tggctttggc cctggcaaga tggattccag ggggtgagcac 1620
agacaggatc gcaggagag gccgtattaa ttagcctggc tcccagggtt ctggaacagc 1680
tttttgcct gtaccagtg ttaccctcgt tattttgtaa cttccaatt cctgatcacc 1740
caagggtttt tttgtgtcgg actatgtaat tgtaactata cctctggttc ccattaaaag 1800
tgaccatttt agttaaaaa aa 1822

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&lt;210&gt; 186

&lt;211&gt; 120

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 186

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tggtttctaa agatgaaatt aagaattggt ccacaagggt taagtgtctg gtggtaaagt 60
tgggctcgga ggcctacagt aacccaaata taagtgccac ggagaaagct aaagcagaga 120

```

&lt;210&gt; 187

&lt;211&gt; 118

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 187

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tgagtgtgtg ggagacaact ccgaatgttt aattctggaa gagggatgta acattgccct 60
gaggattcga gatggtagtg aattgatcta gattggaaac aatggaatta gaagtgtt 118

```

&lt;210&gt; 188

&lt;211&gt; 120

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 188

141/299

gtgtgggaga caactccgaa tgtttaattc tggaagaggg atgtaacatt gccctgagga 60  
 tgggtggctca cacctgtaat cccagcactt tgggagacca gaggtgggtg gatcacctg 120

<210> 189  
 <211> 126  
 <212> PRT  
 <213> Homo sapiens

<400> 189  
 Gln Ser Ser Gln Ser Ser Tyr Gly Gln Gln Ser Ser Tyr Pro Gly Tyr  
 1 5 10 15  
 Gly Gln Gln Pro Ala Pro Ser Ser Thr Ser Gly Ser Tyr Gly Ser Ser  
 20 25 30  
 Ser Gln Ser Ser Ser Tyr Gly Gln Pro Gln Ser Gly Ser Tyr Ser Gln  
 35 40 45  
 Gln Pro Ser Tyr Gly Gly Gln Gln Gln Ser Tyr Gly Gln Gln Gln Ser  
 50 55 60  
 Tyr Asn Pro Pro Gln Gly Tyr Gly Gln Gln Asn Gln Tyr Asn Ser Ser  
 65 70 75 80  
 Ser Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Val Phe Lys Lys Glu Val  
 85 90 95  
 Tyr Leu His Thr Ser Pro Leu Leu Lys Ala Asp Val Leu Phe Gln Thr  
 100 105 110  
 Asp Pro Thr Ala Glu Met Ala Ala Glu Ser Leu Pro Phe Ser  
 115 120 125

<210> 190  
 <211> 377  
 <212> DNA  
 <213> Homo sapiens

<400> 190  
 cagagctccc aatcgtctta cgggcagcag tcctcctacc ctggctatgg ccagcagcca 60  
 gctcccagca gcacctcggg aagttacggg agcagttctc agagcagcag ctatggggcag 120  
 ccccagagtg ggagctacag ccagcagcct agctatgggtg gacagcagca aagctatgga 180  
 cagcagcaaa gctataatcc ccctcagggc tatggacagc agaaccagta caacagcagc 240  
 agtgggtgggtg gaggtggagg tggaggtgga gtgttcaaga aggaagtgtg tcttcataca 300  
 tcaccactcc tgaaagcaga tgtgtttttc cagactgatc caactgcaga gatggcagct 360  
 gagtcattgc ctttctc 377

<210> 191  
 <211> 689  
 <212> PRT  
 <213> Homo sapiens

<400> 191  
 Pro Ser Val Ser Ser Ile Ser Arg Ile Leu Arg Ser Lys Phe Gly Lys  
 1 5 10 15

Gly	Glu	Glu	Glu	Glu	Ala	Asp	Leu	Glu	Arg	Lys	Glu	Ala	Glu	Glu	Ser	
			20				25						30			
Glu	Lys	Lys	Ala	Lys	His	Ser	Ile	Asp	Gly	Ile	Leu	Ser	Glu	Arg	Ala	
			35				40						45			
Ser	Ala	Pro	Gln	Ser	Asp	Glu	Gly	Ser	Asp	Ile	Asp	Ser	Glu	Pro	Asp	
			50				55						60			
Leu	Pro	Leu	Lys	Arg	Lys	Gln	Arg	Arg	Ser	Arg	Thr	Thr	Phe	Thr	Ala	
			65				70						75			
Glu	Gln	Leu	Glu	Glu	Leu	Glu	His	Val	Ala	Phe	Glu	Arg	Thr	His	Tyr	
			85						90						95	
Pro	Asp	Ile	Tyr	Thr	Arg	Glu	Glu	Leu	Ala	Gln	Arg	Ala	Lys	Leu	Thr	
			100			105						110				
Glu	Ala	Arg	Val	Gln	Val	Trp	Phe	Ser	Asn	Arg	Arg	Ala	Arg	Trp	Arg	
			115			120						125				
Lys	Gln	Ala	Gly	Ala	Asn	Gln	Leu	Met	Ala	Phe	Asn	His	Leu	Ile	Pro	
			130			135						140				
Gly	Gly	Phe	Pro	Pro	Thr	Ala	Met	Pro	Thr	Leu	Pro	Thr	Tyr	Gln	Leu	
			145			150						155			160	
Ser	Glu	His	Ser	Tyr	Gln	Pro	Thr	Ser	Ile	Pro	Gln	Ala	Val	Ser	Asp	
			165			170						175				
Pro	Ser	Ser	Thr	Val	His	Arg	Pro	Gln	Pro	Leu	Pro	Pro	Ser	Thr	Val	
			180			185						190				
His	Gln	Ser	Thr	Ile	Pro	Ser	Asn	Pro	Asp	Ser	Ser	Ser	Ala	Tyr	Cys	
			195			200						205				
Leu	Pro	Ser	Thr	Arg	His	Gly	Phe	Ser	Ser	Tyr	Thr	Asp	Ser	Phe	Val	
			210			215						220				
Pro	Pro	Ser	Gly	Pro	Ser	Asn	Pro	Met	Asn	Pro	Thr	Ile	Gly	Asn	Gly	
			225			230						235			240	
Leu	Ser	Pro	Gln	Asn	Ser	Ile	Arg	His	Asn	Leu	Ser	Leu	His	Ser	Lys	
			245			250						255				
Phe	Ile	Arg	Val	Gln	Asn	Glu	Gly	Thr	Gly	Lys	Ser	Ser	Trp	Trp	Met	
			260			265						270				
Leu	Asn	Pro	Glu	Gly	Gly	Lys	Ser	Gly	Lys	Ser	Pro	Arg	Arg	Arg	Ala	
			275			280						285				
Ala	Ser	Met	Asp	Asn	Asn	Ser	Lys	Phe	Ala	Lys	Ser	Arg	Ser	Arg	Ala	
			290			295						300				
Ala	Lys	Lys	Lys	Ala	Ser	Leu	Gln	Ser	Gly	Gln	Glu	Gly	Ala	Gly	Asp	
			305			310						315			320	

143/299

Ser Pro Gly Ser Gln Phe Ser Lys Trp Pro Ala Ser Pro Gly Ser His  
 325 330 335  
 Ser Asn Asp Asp Phe Asp Asn Trp Ser Thr Phe Arg Pro Arg Thr Ser  
 340 345 350  
 Ser Asn Ala Ser Thr Ile Ser Gly Arg Leu Ser Pro Ile Met Thr Glu  
 355 360 365  
 Gln Asp Asp Leu Gly Glu Gly Asp Val His Ser Met Val Tyr Pro Pro  
 370 375 380  
 Ser Ala Ala Lys Met Ala Ser Thr Leu Pro Ser Leu Ser Glu Ile Ser  
 385 390 395 400  
 Asn Pro Glu Asn Met Glu Asn Leu Leu Asp Asn Leu Asn Leu Leu Ser  
 405 410 415  
 Ser Pro Thr Ser Leu Thr Val Ser Thr Gln Ser Ser Pro Gly Thr Met  
 420 425 430  
 Met Gln Gln Thr Pro Cys Tyr Ser Phe Ala Pro Pro Asn Thr Ser Leu  
 435 440 445  
 Asn Ser Pro Ser Pro Asn Tyr Gln Lys Tyr Thr Tyr Gly Gln Ser Ser  
 450 455 460  
 Met Ser Pro Leu Pro Gln Met Pro Ile Gln Thr Leu Gln Asp Asn Lys  
 465 470 475 480  
 Ser Ser Tyr Gly Gly Met Ser Gln Tyr Asn Cys Ala Pro Gly Leu Leu  
 485 490 495  
 Lys Glu Leu Leu Thr Ser Asp Ser Pro Pro His Asn Asp Ile Met Thr  
 500 505 510  
 Pro Val Asp Pro Gly Val Ala Gln Pro Asn Ser Arg Val Leu Gly Gln  
 515 520 525  
 Asn Val Met Met Gly Pro Asn Ser Val Met Ser Thr Tyr Gly Ser Gln  
 530 535 540  
 Ala Ser His Asn Lys Met Met Asn Pro Ser Ser His Thr His Pro Gly  
 545 550 555 560  
 His Ala Gln Gln Thr Ser Ala Val Asn Gly Arg Pro Leu Pro His Thr  
 565 570 575  
 Val Ser Thr Met Pro His Thr Ser Gly Met Asn Arg Leu Thr Gln Val  
 580 585 590  
 Lys Thr Pro Val Gln Val Pro Leu Pro His Pro Met Gln Met Ser Ala  
 595 600 605  
 Leu Gly Gly Tyr Ser Ser Val Ser Ser Cys Asn Gly Tyr Gly Arg Met  
 610 615 620  
 Gly Leu Leu His Gln Glu Lys Leu Pro Ser Asp Leu Asp Gly Met Phe

144/299

625		630		635		640
Ile Glu Arg Leu Asp Cys Asp Met Glu Ser Ile Ile Arg Asn Asp Leu						
	645			650		655
Met Asp Gly Asp Thr Leu Asp Phe Asn Phe Asp Asn Val Leu Pro Asn						
	660		665		670	
Gln Ser Phe Pro His Ser Val Lys Thr Thr Thr His Ser Trp Val Ser						
	675	680		685		

Gly

&lt;210&gt; 192

&lt;211&gt; 3517

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 192

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ccgtcagtga gttccatcag ccgcctcctg agaagtaa atcgggaaagg tgaagaggag 60
gaggccgact tggagaggaa ggaggcagag gaaagcgaga agaaggccaa acacagcatc 120
gacggcatcc tgagcgagcg agcctcagca cccaatcag atgaaggctc tgatattgac 180
tctgaaccag atttaccact aaagaggaaa cagcgagaa gccgaaccac cttcacagca 240
gaacagctgg aggaactgga gcacgttgct tttgagagaa ctcatcacc tgacatttat 300
actagggagg aactggccca gagggcgagg ctccaggagg ccgagtaga ggtctgggtt 360
agcaaccgcc gtgcaagatg gaggaagcaa gctggggcca atcaactgat ggctttcaac 420
catctcattc ccgggggatt ccctccact gccatgccga ccttgccaac gtaccagctg 480
tcggagcact cttaccagcc cacatctatt ccacaagctg tgtcagatcc cagcagcacc 540
gttcacagac ctcaaccgct tcctccaagc actgtacacc aaagcagcat tccttccaac 600
ccagacagca gctctgccta ctgcctcccc agcaccaggc atggattttc cagctataca 660
gacagctttg tgctcctgtc ggggccctcc aaccccatga accccaccat tggcaatggc 720
ctctcacctc agaattcaat tcgtcataat ctgtccctac acagcaagtt cattcgtgtg 780
cagaatgaag gaactggaaa aagttcttgg tggatgctca atccagaggg tggcaagagc 840
gggaaatctc ctaggagaag agctgcatcc atggacaaca acagtaaatt tgctaagagc 900
cgaagccgag ctgccaagaa gaaagcatct ctccagtcgt gccaggaggg tgctggggac 960
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gtgtaccgac catctgccgc aaagatggcc tctactttac ccagtctgtc tgagataaag 1200
aatcccgaaa acatggaaaa tcttttggat aatctcaacc ttctctcatc accaacatca 1260
ttaactgttt cgaccagtc ctcacctggc accatgatgc agcagacgcc gtgctactcg 1320
tttgcgccac caaacaccag tttgaattca ccagcccaa actacaaaa atatacatat 1380
ggccaatcca gcatgagccc tttgccccag atgcctatac aaacacttca ggacaataag 1440
tcgagttatg gaggtatgag tcagtataac tgtgcgcctg gactcttgaa ggagttgctg 1500
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cttcagattg tctgacagca ggaactgaga gaagcagtc aaagatgtct ttcaccaact 2160
cccttttagt tttcttgggt aaaaaaaaaa acaaaaaaaaaa aaacctcct tttttcctt 2220
cgtcagactt ggcagcaaag acatttttcc tgtacaggat gtttgcccaa tgtgtgcagg 2280

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145/299

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ttatgtgctg ctgtagataa ggactgtgcc attggaaatt tcattacaat gaagtgccaa 2340
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gtatataagc agtagataca gattgtatgt gtgtgtgttt ttggtttttc taaatatcca 2460
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ttaaatacatt gtaattagta cttgcatatt caacgtttca ggccctgggtt gggcaggaaa 3120
gtgatgtata gttatggaca ctttgcgttt cttatttagg ataacttaat atgtttttat 3180
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tttgagttga gcttttagcaa agttttccct cataattctt tgctcttggt tcagtcagg 3420
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ttctcccttc tgcctgcag attagattac ttagcac 3517

```

&lt;210&gt; 193

&lt;211&gt; 55

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 193

```

Pro Tyr Gly Tyr Asp Gln Ser Pro Phe Met Cys Asn Lys Arg Ala Glu
  1                      5                      10          15

```

```

Asp Phe Gln Gly Asn Asp Leu Asp Asn Asp Pro Asn Arg Gly Asn Gln
      20                      25                      30

```

```

Val Glu Arg Pro Gln Met Thr Phe Gly Arg Leu Gln Gly Ile Ser Pro
      35                      40                      45

```

```

Lys Ile Met Pro Lys Lys Pro
      50                      55

```

&lt;210&gt; 194

&lt;211&gt; 165

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 194

```

ccttatggat atgaccagtc tcctttcatg tgtaataaac gggccgaaga cttccagggg 60
aatgatttgg ataatgaccc taaccgtggg aatcaggttg aacgtcctca gatgactttc 120
ggcaggctcc agggaatctc cccgaagatc atgcccaaga agcca 165

```

&lt;210&gt; 195

&lt;211&gt; 188

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens



146/299

&lt;400&gt; 195

```

Met Asn Gly Asp Asp Ala Phe Ala Arg Arg Pro Thr Val Gly Ala Gln
 1           5           10           15

Ile Pro Glu Lys Ile Gln Lys Ala Phe Asp Asp Ile Ala Lys Tyr Phe
      20           25           30

Ser Lys Glu Glu Trp Glu Lys Met Lys Ala Ser Glu Lys Ile Phe Tyr
      35           40           45

Val Tyr Met Lys Arg Lys Tyr Glu Ala Met Thr Lys Leu Gly Phe Lys
      50           55           60

Ala Thr Leu Pro Pro Phe Met Cys Asn Lys Arg Ala Glu Asp Phe Gln
      65           70           75           80

Gly Asn Asp Leu Asp Asn Asp Pro Asn Arg Gly Asn Gln Val Glu Arg
      85           90           95

Pro Gln Met Thr Phe Gly Arg Leu Gln Gly Ile Ser Pro Lys Ile Met
      100          105          110

Pro Lys Lys Pro Ala Glu Glu Gly Asn Asp Ser Glu Glu Val Pro Glu
      115          120          125

Ala Ser Gly Pro Gln Asn Asp Gly Lys Glu Leu Cys Pro Pro Gly Lys
      130          135          140

Pro Thr Thr Ser Glu Lys Ile His Glu Arg Ser Gly Pro Lys Arg Gly
      145          150          155          160

Glu His Ala Trp Thr His Arg Leu Arg Glu Arg Lys Gln Leu Val Ile
      165          170          175

Tyr Glu Glu Ile Ser Asp Pro Glu Glu Asp Asp Glu
      180          185

```

&lt;210&gt; 196

&lt;211&gt; 766

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 196

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147/299

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149/299

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151/299

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Val Lys Arg Arg Asp Ser Ala Thr Ser Phe Ser Leu Asp Phe Gly Tyr
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152/299

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155/299

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&lt;210&gt; 202

&lt;211&gt; 198

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 202

156/299

Met Asp Ser Leu Leu Met Asn Arg Arg Lys Phe Leu Tyr Gln Phe Lys  
 1 5 10 15

Asn Val Arg Trp Ala Lys Gly Arg Arg Glu Thr Tyr Leu Cys Tyr Val  
 20 25 30

Val Lys Arg Arg Asp Ser Ala Thr Ser Phe Ser Leu Asp Phe Gly Tyr  
 35 40 45

Leu Arg Asn Lys Asn Gly Cys His Val Glu Leu Leu Phe Leu Arg Tyr  
 50 55 60

Ile Ser Asp Trp Asp Leu Asp Pro Gly Arg Cys Tyr Arg Val Thr Trp  
 65 70 75 80

Phe Thr Ser Trp Ser Pro Cys Tyr Asp Cys Ala Arg His Val Ala Asp  
 85 90 95

Phe Leu Arg Gly Asn Pro Asn Leu Ser Leu Arg Ile Phe Thr Ala Arg  
 100 105 110

Leu Tyr Phe Cys Glu Asp Arg Lys Ala Glu Pro Glu Gly Leu Arg Arg  
 115 120 125

Leu His Arg Ala Gly Val Gln Ile Ala Ile Met Thr Phe Lys Asp Tyr  
 130 135 140

Phe Tyr Cys Trp Asn Thr Phe Val Glu Asn His Glu Arg Thr Phe Lys  
 145 150 155 160

Ala Trp Glu Gly Leu His Glu Asn Ser Val Arg Leu Ser Arg Gln Leu  
 165 170 175

Arg Arg Ile Leu Leu Pro Leu Tyr Glu Val Asp Asp Leu Arg Asp Ala  
 180 185 190

Phe Arg Thr Leu Gly Leu  
 195

&lt;210&gt; 203

&lt;211&gt; 2791

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 203

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 caaaaatgtc cgctgggcta agggctcggcg tgagacctac ctgtgctacg tagtgaagag 180  
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157/299

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aataaaaaat cagtatgatg gaataaactt g' 2791

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&lt;210&gt; 204

&lt;211&gt; 198

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 204

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Met Asp Ser Leu Leu Met Asn Arg Arg Lys Phe Leu Tyr Gln Phe Lys
  1             5             10             15

Asn Val Arg Trp Ala Lys Gly Arg Arg Glu Thr Tyr Leu Cys Tyr Val
      20             25             30

Val Lys Arg Arg Asp Ser Ala Thr Ser Phe Ser Leu Asp Phe Gly Tyr
      35             40             45

Leu Arg Asn Lys Asn Gly Cys His Val Glu Leu Leu Phe Leu Arg Tyr
      50             55             60

Ile Ser Asp Trp Asp Leu Asp Pro Gly Arg Cys Tyr Arg Val Thr Trp
      65             70             75             80

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[illegible]

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<210> 205
<211> 2791
<212> DNA
<213> Homo sapiens
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<400> 205						
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caaaaatgtc	cgctgggcta	agggctcggcg	tgagacctac	ctgtgctacg	tagtgaagag	180
gcgtgacagt	gctacatcta	tttcaactga	ctttggttat	cttcgcaata	agaacggctg	240
ccacgtggaa	ttgctctctc	tccgtctacat	ctcggacttg	gacctagacc	ctggccgctg	300
ctaccgcgtc	acctggttca	cctcctggag	ccctcgctac	gactgtgcc	gacatgtggc	360
cgactttctg	cgagggaacc	ccaacctcag	tctgaggatc	ttcacccgc	gcctctactt	420
ctgtgaggac	cgcaaggctg	agcccagagg	gctgcggcgg	ctgcaccgcg	ccgggggtgca	480
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aacaattgga	aggaagtgtg	ttgaattgtg	gggagaggaa	aatctattgg	ctctcgtggg	1560
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159/299

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aataaaaaat cagtatgatg gaataaaactt g 2791

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&lt;210&gt; 206

&lt;211&gt; 416

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 206

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Pro Asn Ser Asn His Val Ala Ser Gly Ala Gly Glu Ala Ala Ile Glu
  1              5              10              15

Thr Gln Ser Ser Ser Ser Glu Glu Ile Val Pro Ser Pro Pro Ser Pro
          20              25              30

Pro Pro Leu Pro Arg Ile Tyr Lys Pro Cys Phe Val Cys Gln Asp Lys
          35              40              45

Ser Ser Gly Tyr His Tyr Gly Val Ser Ala Cys Glu Gly Cys Lys Gly
          50              55              60

Phe Phe Arg Arg Ser Ile Gln Lys Asn Met Val Tyr Thr Cys His Arg
          65              70              75              80

Asp Lys Asn Cys Ile Ile Asn Lys Val Thr Arg Asn Arg Cys Gln Tyr
          85              90              95

Cys Arg Leu Gln Lys Cys Phe Glu Val Gly Met Ser Lys Glu Ser Val
          100             105             110

Arg Asn Asp Arg Asn Lys Lys Lys Lys Glu Val Pro Lys Pro Glu Cys
          115             120             125

Ser Glu Ser Tyr Thr Leu Thr Pro Glu Val Gly Glu Leu Ile Glu Lys
          130             135             140

Val Arg Lys Ala His Gln Glu Thr Phe Pro Ala Leu Cys Gln Leu Gly
          145             150             155             160

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160/299

Lys Tyr Thr Thr Asn Asn Ser Ser Glu Gln Arg Val Ser Leu Asp Ile  
 165 170 175  
 Asp Leu Trp Asp Lys Phe Ser Glu Leu Ser Thr Lys Cys Ile Ile Lys  
 180 185 190  
 Thr Val Glu Phe Ala Lys Gln Leu Pro Gly Phe Thr Thr Leu Thr Ile  
 195 200 205  
 Ala Asp Gln Ile Thr Leu Leu Lys Ala Ala Cys Leu Asp Ile Leu Ile  
 210 215 220  
 Leu Arg Ile Cys Thr Arg Tyr Thr Pro Glu Gln Asp Thr Met Thr Phe  
 225 230 235 240  
 Ser Asp Gly Leu Thr Leu Asn Arg Thr Gln Met His Asn Ala Gly Phe  
 245 250 255  
 Gly Pro Leu Thr Asp Leu Val Phe Ala Phe Ala Asn Gln Leu Leu Pro  
 260 265 270  
 Leu Glu Met Asp Asp Ala Glu Thr Gly Leu Leu Ser Ala Ile Cys Leu  
 275 280 285  
 Ile Cys Gly Asp Arg Gln Asp Leu Glu Gln Pro Asp Arg Val Asp Met  
 290 295 300  
 Leu Gln Glu Pro Leu Leu Glu Ala Leu Lys Val Tyr Val Arg Lys Arg  
 305 310 315 320  
 Arg Pro Ser Arg Pro His Met Phe Pro Lys Met Leu Met Lys Ile Thr  
 325 330 335  
 Asp Leu Arg Ser Ile Ser Ala Lys Gly Ala Glu Arg Val Ile Thr Leu  
 340 345 350  
 Lys Met Glu Ile Pro Gly Ser Met Pro Pro Leu Ile Gln Glu Met Leu  
 355 360 365  
 Glu Asn Ser Glu Gly Leu Asp Thr Leu Ser Gly Gln Pro Gly Gly Gly  
 370 375 380  
 Gly Arg Asp Gly Gly Gly Leu Ala Pro Pro Pro Gly Ser Cys Ser Pro  
 385 390 395 400  
 Ser Leu Ser Pro Ser Ser Asn Arg Ser Ser Pro Ala Thr His Ser Pro  
 405 410 415

&lt;210&gt; 207

&lt;211&gt; 1284

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 207

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 ccttgctttg tctgtcagga caagtcctca ggctaccact atggggtcag cgctgtgag 180

161/299

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&lt;210&gt; 208

&lt;211&gt; 797

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 208

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Met Glu Pro Ala Pro Ala Arg Ser Pro Arg Pro Gln Gln Asp Pro Ala
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Arg Pro Gln Glu Pro Thr Met Pro Pro Pro Glu Thr Pro Ser Glu Gly
          20              25              30

Arg Gln Pro Ser Pro Ser Pro Ser Pro Thr Glu Arg Ala Pro Ala Ser
  35              40              45

Glu Glu Glu Phe Gln Phe Leu Arg Cys Gln Gln Cys Gln Ala Glu Ala
  50              55              60

Lys Cys Pro Lys Leu Leu Pro Cys Leu His Thr Leu Cys Ser Gly Cys
  65              70              75              80

Leu Glu Ala Ser Gly Met Gln Cys Pro Ile Cys Gln Ala Pro Trp Pro
          85              90              95

Leu Gly Ala Asp Thr Pro Ala Leu Asp Asn Val Phe Phe Glu Ser Leu
          100              105              110

Gln Arg Arg Leu Ser Val Tyr Arg Gln Ile Val Asp Ala Gln Ala Val
          115              120              125

Cys Thr Arg Cys Lys Glu Ser Ala Asp Phe Trp Cys Phe Glu Cys Glu
          130              135              140

Gln Leu Leu Cys Ala Lys Cys Phe Glu Ala His Gln Trp Phe Leu Lys
          145              150              155              160

His Glu Ala Arg Pro Leu Ala Glu Leu Arg Asn Gln Ser Val Arg Glu

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162/299

				165				170				175			
Phe	Leu	Asp	Gly	Thr	Arg	Lys	Thr	Asn	Asn	Ile	Phe	Cys	Ser	Asn	Pro
			180				185						190		
Asn	His	Arg	Thr	Pro	Thr	Leu	Thr	Ser	Ile	Tyr	Cys	Arg	Gly	Cys	Ser
		195				200						205			
Lys	Pro	Leu	Cys	Cys	Ser	Cys	Ala	Leu	Leu	Asp	Ser	Ser	His	Ser	Glu
		210				215						220			
Leu	Lys	Cys	Asp	Ile	Ser	Ala	Glu	Ile	Gln	Gln	Arg	Gln	Glu	Glu	Leu
225				230						235			240		
Asp	Ala	Met	Thr	Gln	Ala	Leu	Gln	Glu	Gln	Asp	Ser	Ala	Phe	Gly	Ala
			245				250						255		
Val	His	Ala	Gln	Met	His	Ala	Ala	Val	Gly	Gln	Leu	Gly	Arg	Ala	Arg
			260				265						270		
Ala	Glu	Thr	Glu	Glu	Leu	Ile	Arg	Glu	Arg	Val	Arg	Gln	Val	Val	Ala
			275				280						285		
His	Val	Arg	Ala	Gln	Glu	Arg	Glu	Leu	Leu	Glu	Ala	Val	Asp	Ala	Arg
		290				295						300			
Tyr	Gln	Arg	Asp	Tyr	Glu	Glu	Met	Ala	Ser	Arg	Leu	Gly	Arg	Leu	Asp
305				310						315			320		
Ala	Val	Leu	Gln	Arg	Ile	Arg	Thr	Gly	Ser	Ala	Leu	Val	Gln	Arg	Met
			325				330						335		
Lys	Cys	Tyr	Ala	Ser	Asp	Gln	Glu	Val	Leu	Asp	Met	His	Gly	Phe	Leu
			340				345						350		
Arg	Gln	Ala	Leu	Cys	Arg	Leu	Arg	Gln	Glu	Glu	Pro	Gln	Ser	Leu	Gln
			355				360						365		
Ala	Ala	Val	Arg	Thr	Asp	Gly	Phe	Asp	Glu	Phe	Lys	Val	Arg	Leu	Gln
			370				375						380		
Asp	Leu	Ser	Ser	Cys	Ile	Thr	Gln	Gly	Lys	Ala	Ile	Glu	Thr	Gln	Ser
385				390						395			400		
Ser	Ser	Ser	Glu	Glu	Ile	Val	Pro	Ser	Pro	Pro	Ser	Pro	Pro	Pro	Leu
			405				410						415		
Pro	Arg	Ile	Tyr	Lys	Pro	Cys	Phe	Val	Cys	Gln	Asp	Lys	Ser	Ser	Gly
			420				425						430		
Tyr	His	Tyr	Gly	Val	Ser	Ala	Cys	Glu	Gly	Cys	Lys	Gly	Phe	Phe	Arg
		435				440						445			
Arg	Ser	Ile	Gln	Lys	Asn	Met	Val	Tyr	Thr	Cys	His	Arg	Asp	Lys	Asn
			450				455						460		
Cys	Ile	Ile	Asn	Lys	Val	Thr	Arg	Asn	Arg	Cys	Gln	Tyr	Cys	Arg	Leu
465				470						475			480		

163/299

Gln	Lys	Cys	Phe	Glu	Val	Gly	Met	Ser	Lys	Glu	Ser	Val	Arg	Asn	Asp		
				485					490						495		
Arg	Asn	Lys	Lys	Lys	Lys	Glu	Val	Pro	Lys	Pro	Glu	Cys	Ser	Glu	Ser		
			500					505					510				
Tyr	Thr	Leu	Thr	Pro	Glu	Val	Gly	Glu	Leu	Ile	Glu	Lys	Val	Arg	Lys		
		515					520					525					
Ala	His	Gln	Glu	Thr	Phe	Pro	Ala	Leu	Cys	Gln	Leu	Gly	Lys	Tyr	Thr		
	530					535					540						
Thr	Asn	Asn	Ser	Ser	Glu	Gln	Arg	Val	Ser	Leu	Asp	Ile	Asp	Leu	Trp		
545					550					555					560		
Asp	Lys	Phe	Ser	Glu	Leu	Ser	Thr	Lys	Cys	Ile	Ile	Lys	Thr	Val	Glu		
				565					570					575			
Phe	Ala	Lys	Gln	Leu	Pro	Gly	Phe	Thr	Thr	Leu	Thr	Ile	Ala	Asp	Gln		
			580					585					590				
Ile	Thr	Leu	Leu	Lys	Ala	Ala	Cys	Leu	Asp	Ile	Leu	Ile	Leu	Arg	Ile		
		595					600					605					
Cys	Thr	Arg	Tyr	Thr	Pro	Glu	Gln	Asp	Thr	Met	Thr	Phe	Ser	Asp	Gly		
	610					615					620						
Leu	Thr	Leu	Asn	Arg	Thr	Gln	Met	His	Asn	Ala	Gly	Phe	Gly	Pro	Leu		
625					630					635					640		
Thr	Asp	Leu	Val	Phe	Ala	Phe	Ala	Asn	Gln	Leu	Leu	Pro	Leu	Glu	Met		
				645					650					655			
Asp	Asp	Ala	Glu	Thr	Gly	Leu	Leu	Ser	Ala	Ile	Cys	Leu	Ile	Cys	Gly		
			660					665					670				
Asp	Arg	Gln	Asp	Leu	Glu	Gln	Pro	Asp	Arg	Val	Asp	Met	Leu	Gln	Glu		
		675					680					685					
Pro	Leu	Leu	Glu	Ala	Leu	Lys	Val	Tyr	Val	Arg	Lys	Arg	Arg	Pro	Ser		
	690					695					700						
Arg	Pro	His	Met	Phe	Pro	Lys	Met	Leu	Met	Lys	Ile	Thr	Asp	Leu	Arg		
705					710					715					720		
Ser	Ile	Ser	Ala	Lys	Gly	Ala	Glu	Arg	Val	Ile	Thr	Leu	Lys	Met	Glu		
				725					730					735			
Ile	Pro	Gly	Ser	Met	Pro	Pro	Leu	Ile	Gln	Glu	Met	Leu	Glu	Asn	Ser		
			740					745					750				
Glu	Gly	Leu	Asp	Thr	Leu	Ser	Gly	Gln	Pro	Gly	Gly	Gly	Gly	Arg	Asp		
		755					760					765					
Gly	Gly	Gly	Leu	Ala	Pro	Pro	Pro	Gly	Ser	Cys	Ser	Pro	Ser	Leu	Ser		
		770				775					780						

164/299

Pro Ser Ser Asn Arg Ser Ser Pro Ala Thr His Ser Pro  
 785 790 795

<210> 209  
 <211> 3036  
 <212> DNA  
 <213> Homo sapiens

<400> 209  
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 ggggtccatgg agcctgcacc cgcccgatct ccgaggcccc agcaggaccc cgcccggccc 120  
 caggagccca ccatgcctcc ccccgagacc ccctctgaag gccgccagcc cagccccagc 180  
 cccagcccta cagagcgagc ccccgcttcg gaggaggagt tccagtttct gcgctgccag 240  
 caatgccagg cggaagccaa gtgcccgaag ctgctgcctt gtctgcacac gctgtgctca 300  
 ggatgcctgg aggcgtcggg catgcagtgc cccatctgcc aggcgcccctg gcccctaggt 360  
 gcagacacac ccgcccctgga taacgtcttt ttcgagagtc tgcagcggcg cctgtcggtg 420  
 taccggcaga ttgtggatgc gcaggctgtg tgcacccgct gcaaagagtc ggccgacttc 480  
 tgggtgctttg agtgcgagca gctcctctgc gccaaagtgt tgcaggcaca ccagtggttc 540  
 ctcaagcacg agggcccgcc cctagcagag ctgcgcaacc agtcgggtgc tgagtctctg 600  
 gacggcaccg gcaagaccaa caacatcttc tgctccaacc ccaaccaccc caccctacg 660  
 ctgaccagca tctactgccg aggatgttcc aagccgctgt gctgctcgtg cgcgctcctt 720  
 gacagcagcc acagtgcgct caagtgcgac atcagcgcag agatccagca gcgacaggag 780  
 gagctggacg ccatgacgca ggcgctgcag gagcaggata gtgccttttg ccggtttcac 840  
 gcgcagatgc acgcggccgt cggccagctg ggccgcgcgc gtgccgagac cgaggagctg 900  
 atccgcgagc gcgtgcgcca ggtggtagct cacgtgcggg ctcaggagcg cgagctgctg 960  
 gaggtgtgtg acgcgcggtt ccagcgcgac tacgaggaga tggccagtcg gctgggcccgc 1020  
 ctggatgctg tgcctgcagc catccgcacg ggcagcgcgc tgggtgcagag gatgaagtgc 1080  
 tacgcctcgg accaggaggt gctggacatg cacggtttcc tgcgccagcc gctctgcgcg 1140  
 ctgcgccagg aggcgccccg gagcctgcaa gctgcctgac gcaccgatgg cttcgacgag 1200  
 ttcaaggtgc gcctgcagga cctcagctct tgcctcacc aggggaaagc cattgagacc 1260  
 cagagcagca gttctgaaga gatagtggcc agcctcctcc cgccaccccc tctacccccg 1320  
 atctacaagc cttgctttgt ctgtcaggac aagtcctcag gctaccacta tggggctcagc 1380  
 gcctgtgagg gctgcaaggc cttcttccgc cgcagcatcc agaagaacat ggtgtacacg 1440  
 tgtcaccggg acaagaactg catcatcaac aaggtgaccc ggaaccgctg ccagtactgc 1500  
 cgactgcaga agtgctttga agtgggcatg tccaaggagt ctgtgagaaa cgaccgaaac 1560  
 aagaagaaga aggaggtgcc caagcccag tgccttgaga gctacacgt gacgcggag 1620  
 gtggggggagc tcattgagaa ggtgcgcaaa gcgcaccag aaaccttccc tgccctctgc 1680  
 cagctggggc aatacactac gaacaacagc tcagaacaac gtgtctctct ggacattgac 1740  
 ctctgggaca agttcagtga actctccacc aagtgcacaa ttaagactgt ggagttcgcc 1800  
 aagcagctgc ccggtttcac caccctcacc atcgccgacc agatcaccct cctcaaggct 1860  
 gcctgcctgg acatcctgat cctgcggatc tgcacgcggg acacgcccga gcaggacacc 1920  
 atgaccttct cggacgggct gaccctgaac cggaccaga tgcacaacgc tggcttcggc 1980  
 cccctcaccg acctgggtct tgccttcgcc aaccagctgc tgcccctgga gatggatgat 2040  
 gcggagacgg ggctgctcag cgccatctgc ctcatctgcg gagaccgcca ggacctggag 2100  
 cagccggacc ggggtggacat gctgcaggag ccgctgctgg aggcgctaaa ggtctacgtg 2160  
 cggaagcggg gggccagccg ccccccacatg ttccccaaga tgctaataaa gattactgac 2220  
 ctgcgaagca tcagcgccaa gggggctgag cgggtgatca cgctgaagat ggagatccc 2280  
 ggctccatgc cgcctctcat ccaggaaaatg ttggagaact cagagggcct ggacactctg 2340  
 agcggacagc cgggggggtg ggggcgggac ggggggtggc tggccccccc gccaggcagc 2400  
 tgtagcccca gcctcagccc cagctccaac agaagcagcc cggccaccca ctcccctgta 2460  
 ccgcccacgc cacatggaca cagccctcgc cctccgcccc ggctttttct tgcctttcta 2520  
 ccgaccatgt gaccccgac cagccctgcc cccacctgcc ctcccgggca gtactgggga 2580  
 ccttccctgg gggacgggga gggaggaggc agcgactcct tggacagagg cctggggcct 2640  
 cagtggactg cctgctccca cagcctgggc tgacgtcaga ggccgaggcc aggaactgag 2700  
 tgagggccct ggctcctggg ctcaggatgg gtcttgggg cctcgtgttc atcaagacac 2760  
 cctctgccc atctcaccac atcttcac caagcaaac ccaggacttg gctcccccat 2820  
 cctcagaact cacaagccat tgctccccag ctggggaacc tcaacctccc cctgcctcgc 2880

165/299

ggttggtgaca gaggggggtgg gacaggggag ggggggttccc cctgtacata ccctgccata 2940  
 ccaaccccag gtattaattc tcgctgggtt tgtttttatt ttaatttttt tgttttgatt 3000  
 tttttaataa gaattttcat tttaagcaaa aaaaaa 3036

<210> 210  
 <211> 99  
 <212> PRT  
 <213> Homo sapiens

<400> 210  
 Asp Val Ser Asn Thr Thr Thr Ala Gln Lys Arg Lys Cys Ser Gln Thr  
 1 5 10 15  
 Gln Cys Pro Arg Lys Val Ile Lys Met Glu Ser Glu Glu Gly Lys Glu  
 20 25 30  
 Ala Arg Leu Ala Leu Pro Ala Pro Gly Pro Tyr Ser Thr Pro Leu Arg  
 35 40 45  
 Thr Pro Leu Trp Asn Gly Ser Asn His Ser Ile Glu Thr Gln Ser Ser  
 50 55 60  
 Ser Ser Glu Glu Ile Val Pro Ser Pro Pro Ser Pro Pro Pro Leu Pro  
 65 70 75 80  
 Arg Ile Tyr Lys Pro Cys Phe Val Cys Gln Asp Lys Ser Ser Gly Tyr  
 85 90 95  
 His Tyr Gly

<210> 211  
 <211> 296  
 <212> DNA  
 <213> Homo sapiens

<400> 211  
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 aaggtcatca agatggagtc tgaggagggg aaggaggcaa gggtggctct cccgccccg 120  
 ggtccgtact ccaccccgct ccggactccg ctttggaaatg gctcaaacca ctccattgag 180  
 acccagagca gcagttctga agagatagtg cccagccctc cctcgccacc ccctctaccc 240  
 cgcactctaca agccttgctt tgtctgtcag gacaagtcct caggctacca ctatgg 296

<210> 212  
 <211> 673  
 <212> PRT  
 <213> Homo sapiens

<400> 212  
 Met Asp Leu Thr Lys Met Gly Met Ile Gln Leu Gln Asn Pro Ser His  
 1 5 10 15  
 Pro Thr Gly Leu Leu Cys Lys Ala Asn Gln Met Arg Leu Ala Gly Thr  
 20 25 30  
 Leu Cys Asp Val Val Ile Met Val Asp Ser Gln Glu Phe His Ala His

166/299

35					40					45						
Arg	Thr	Val	Leu	Ala	Cys	Thr	Ser	Lys	Met	Phe	Glu	Ile	Leu	Phe	His	
50					55					60						
Arg	Asn	Ser	Gln	His	Tyr	Thr	Leu	Asp	Phe	Leu	Ser	Pro	Lys	Thr	Phe	
65					70					75					80	
Gln	Gln	Ile	Leu	Glu	Tyr	Ala	Tyr	Thr	Ala	Thr	Leu	Gln	Ala	Lys	Ala	
85					90					95						
Glu	Asp	Leu	Asp	Asp	Leu	Leu	Tyr	Ala	Ala	Glu	Ile	Leu	Glu	Ile	Glu	
100					105					110						
Tyr	Leu	Glu	Glu	Gln	Cys	Leu	Lys	Met	Leu	Glu	Thr	Ile	Gln	Ala	Ser	
115					120					125						
Asp	Asp	Asn	Asp	Thr	Glu	Ala	Thr	Met	Ala	Asp	Gly	Gly	Ala	Glu	Glu	
130					135					140						
Glu	Glu	Asp	Arg	Lys	Ala	Arg	Tyr	Leu	Lys	Asn	Ile	Phe	Ile	Ser	Lys	
145					150					155					160	
His	Ser	Ser	Glu	Glu	Ser	Gly	Tyr	Ala	Ser	Val	Ala	Gly	Gln	Ser	Leu	
165					170					175						
Pro	Gly	Pro	Met	Val	Asp	Gln	Ser	Pro	Ser	Val	Ser	Thr	Ser	Phe	Gly	
180					185					190						
Leu	Ser	Ala	Met	Ser	Pro	Thr	Lys	Ala	Ala	Val	Asp	Ser	Leu	Met	Thr	
195					200					205						
Ile	Gly	Gln	Ser	Leu	Leu	Gln	Gly	Thr	Leu	Gln	Pro	Pro	Ala	Gly	Pro	
210					215					220						
Glu	Glu	Pro	Thr	Leu	Ala	Gly	Gly	Gly	Arg	His	Pro	Gly	Val	Ala	Glu	
225					230					235					240	
Val	Lys	Thr	Glu	Met	Met	Gln	Val	Asp	Glu	Val	Pro	Ser	Gln	Asp	Ser	
245					250					255						
Pro	Gly	Ala	Ala	Glu	Ser	Ser	Ile	Ser	Gly	Gly	Met	Gly	Asp	Lys	Val	
260					265					270						
Glu	Glu	Arg	Gly	Lys	Glu	Gly	Pro	Gly	Thr	Pro	Thr	Arg	Ser	Ser	Val	
275					280					285						
Ile	Thr	Ser	Ala	Arg	Glu	Leu	His	Tyr	Gly	Arg	Glu	Glu	Ser	Ala	Glu	
290					295					300						
Gln	Val	Pro	Pro	Pro	Ala	Glu	Ala	Gly	Gln	Ala	Pro	Thr	Gly	Arg	Pro	
305					310					315					320	
Glu	His	Pro	Ala	Pro	Pro	Pro	Glu	Lys	His	Leu	Gly	Ile	Tyr	Ser	Val	
325					330					335						
Leu	Pro	Asn	His	Lys	Ala	Asp	Ala	Val	Leu	Ser	Met	Pro	Ser	Ser	Val	
340					345					350						

167/299

Thr Ser Gly Leu His Val Gln Pro Ala Leu Ala Val Ser Met Asp Phe  
 355 360 365  
 Ser Thr Tyr Gly Gly Leu Leu Pro Gln Gly Phe Ile Gln Arg Glu Leu  
 370 375 380  
 Phe Ser Lys Leu Gly Glu Leu Ala Val Gly Met Lys Ser Glu Ser Arg  
 385 390 395 400  
 Thr Ile Gly Glu Gln Cys Ser Val Cys Gly Val Glu Leu Pro Asp Asn  
 405 410 415  
 Glu Ala Val Glu Gln His Arg Lys Leu His Ser Gly Met Lys Thr Tyr  
 420 425 430  
 Gly Cys Glu Leu Cys Gly Lys Arg Phe Leu Asp Ser Leu Arg Leu Arg  
 435 440 445  
 Met His Leu Leu Ala His Ser Ala Gly Ala Lys Ala Phe Val Cys Asp  
 450 455 460  
 Gln Cys Gly Ala Gln Phe Ser Lys Glu Asp Ala Leu Glu Thr His Arg  
 465 470 475 480  
 Gln Thr His Thr Gly Thr Asp Met Ala Val Phe Cys Leu Leu Cys Gly  
 485 490 495  
 Lys Arg Phe Gln Ala Gln Ser Ala Leu Gln Gln His Met Glu Val His  
 500 505 510  
 Ala Gly Val Arg Ser Tyr Ile Cys Ser Glu Cys Asn Arg Thr Phe Pro  
 515 520 525  
 Ser His Thr Ala Leu Lys Arg His Leu Arg Ser His Thr Gly Asp His  
 530 535 540  
 Pro Tyr Glu Cys Glu Phe Cys Gly Ser Cys Phe Arg Asp Glu Ser Thr  
 545 550 555 560  
 Leu Lys Ser His Lys Arg Ile His Thr Gly Glu Lys Pro Tyr Glu Cys  
 565 570 575  
 Asn Gly Cys Asp Lys Lys Phe Ser Leu Lys His Gln Leu Glu Thr His  
 580 585 590  
 Tyr Arg Val His Thr Gly Glu Lys Pro Phe Glu Cys Lys Leu Cys His  
 595 600 605  
 Gln Arg Ser Arg Asp Tyr Ser Ala Met Ile Lys His Leu Arg Thr His  
 610 615 620  
 Asn Gly Ala Ser Pro Tyr Gln Cys Thr Ile Cys Thr Glu Tyr Cys Pro  
 625 630 635 640  
 Ser Leu Ser Ser Met Gln Lys His Met Lys Gly His Lys Pro Glu Glu  
 645 650 655

168/299

Ile Pro Pro Asp Trp Arg Ile Glu Lys Thr Tyr Leu Tyr Leu Cys Tyr  
 660 665 670

Val

<210> 213  
 <211> 2197  
 <212> DNA  
 <213> Homo sapiens

<400> 213  
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 gccgagggga gcaccatgga tctgacaaaa atgggcatga tccagctgca gaaccttagc 120  
 caccacacgg ggctactgtg caaggccaac cagatgcggc tggccgggac tttgtgcgat 180  
 gtggtcatca tgggtggacag ccaggagtgc cagccccacc ggacggtgct ggcttcgacc 240  
 agcaagatgt ttgagatcct cttccaccgc aatagtcaac actatacttt ggacttcctc 300  
 tcgccaaga cttccagca gattctggag tatgcatata cagccacgct gcaagccaag 360  
 gcggaggacc tggatgacct gctgtatgcg gccgagatcc tggagatcga gtacctggag 420  
 gaacagtgc tgaagatgct ggagaccatc caggcctcag acgacaatga caggaggcc 480  
 accatggcgc atggcggggc cgaggaagaa gaggaccgca aggctcggta cctcaagaac 540  
 atcttcatct cgaagcattc cagcaggagg agtgggtatg ccagtgtggc tggacagagc 600  
 ctccctgggc ccatggtgga ccagagccct tcagtctcca cttcatttgg tctttcagcc 660  
 atgagtccca ccaaggctgc agtggacagt ttgatgacca taggacagtc tctcctgcag 720  
 ggaactcttc agccacctgc agggcccgag gagccaactc tggctggggg tgggcggcac 780  
 cctggggtgg ctgaggtgaa gacggagatg atgcaggtgg atgaggtgcc cagccaggac 840  
 agccctgggg cagccgagtc cagcatctca ggaggatgg gggacaaggt tgaggaaaga 900  
 ggcaaagagg ggctgggac cccgactcga agcagcgtca tcaccagtgc tagggagcta 960  
 cactatgggc gagaggagag tgccgagcag gtgccacccc cagctgaggc tggccaggcc 1020  
 cccactgggc gacctgagca cccagcacc cccctgaga agcatctggg catctactcc 1080  
 gtgttgccca accacaaggc tgacgctgta ttgagcatgc cgtcttccgt gacctctggc 1140  
 ctccacgtgc agcctgccct ggctgtctcc atggacttca gcacctatgg ggggctgctg 1200  
 cccagggct tcatccagag ggagctgttc agcaagctgg gggagctggc tgtgggcatg 1260  
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 aacgaggctg tggagcagca caggaagctg cacagtggga tgaagacgta cgggtgagag 1380  
 ctctgcggga agcggttcct ggatagtttg cggctgagaa tgcacttact ggctcattca 1440  
 gcgggtgcca aagcctttgt ctgtgatcag tgcgggtgcac agttttcgaa ggaggatgcc 1500  
 ctggagacac acaggcagac ccatactggc actgacatgg ccgtcttctg tctgctgtgt 1560  
 gggaagcgct tccaggcgca gagcgactg cagcagcaca tggagggtcca cgcgggcgtg 1620  
 cgcagctaca tctgcagtga gtgcaaccgc accttcccca gccacacggc tctcaaacgc 1680  
 cacctgcgct cacatacagg cgaccacccc tacgagtgtg agttctgtgg cagctgcttc 1740  
 cgggatgaga gcacactcaa gagccacaaa cgcattccaca cgggtgagaa accctacgag 1800  
 tgcaatggct gtgacaagaa gttcagcctc aagcatcagc tggagacgca ctatagggtg 1860  
 cacacagggtg agaagccctt tgagtgtgaa ctctgccacc agcgtcccg ggactactcg 1920  
 gccatgatca agcacctgag aacgcacaac ggcgcctcgc cctaccagtg caccatctgc 1980  
 acagagtact gccccagcct ctctccatg cagaagcaca tgaagggcca caagcccag 2040  
 gagatcccgc ccgactggag gatagagaag acgtacctct acctgtgcta tgtgtgaagg 2100  
 gaggcccgcg gcggtggagc cgagcgggga gccaggaaag aagagttgga gtgagatgaa 2160  
 ggaaggacta tgacaaaataa aaaaaaaaaa ggaattc 2197

<210> 214  
 <211> 673  
 <212> PRT  
 <213> Homo sapiens

<400> 214  
 Met Asp Leu Thr Lys Met Gly Met Ile Gln Leu Gln Asn Pro Ser His

169/299

1	5	10	15
Pro Thr Gly Leu Leu Cys Lys Ala Asn Gln Met Arg Leu Ala Gly Thr	20	25	30
Leu Cys Asp Val Val Ile Met Val Asp Ser Gln Glu Phe His Ala His	35	40	45
Arg Thr Val Leu Ala Cys Thr Ser Lys Met Phe Glu Ile Leu Phe His	50	55	60
Arg Asn Ser Gln His Tyr Thr Leu Asp Phe Leu Ser Pro Lys Thr Phe	65	70	75
Gln Gln Ile Leu Glu Tyr Ala Tyr Thr Ala Thr Leu Gln Ala Lys Ala	85	90	95
Glu Asp Leu Asp Asp Leu Leu Tyr Ala Ala Glu Ile Leu Glu Ile Glu	100	105	110
Tyr Leu Glu Glu Gln Cys Leu Lys Met Leu Glu Thr Ile Gln Ala Ser	115	120	125
Asp Asp Asn Asp Thr Glu Ala Thr Met Ala Asp Gly Gly Ala Glu Glu	130	135	140
Glu Glu Asp Arg Lys Ala Arg Tyr Leu Lys Asn Ile Phe Ile Ser Lys	145	150	155
His Ser Ser Glu Glu Ser Gly Tyr Ala Ser Val Ala Gly Gln Ser Leu	165	170	175
Pro Gly Pro Met Val Asp Gln Ser Pro Ser Val Ser Thr Ser Phe Gly	180	185	190
Leu Ser Ala Met Ser Pro Thr Lys Ala Ala Val Asp Ser Leu Met Thr	195	200	205
Ile Gly Gln Ser Leu Leu Gln Gly Thr Leu Gln Pro Pro Ala Gly Pro	210	215	220
Glu Glu Pro Thr Leu Ala Gly Gly Gly Arg His Pro Gly Val Ala Glu	225	230	235
Val Lys Thr Glu Met Met Gln Val Asp Glu Val Pro Ser Gln Asp Ser	245	250	255
Pro Gly Ala Ala Glu Ser Ser Ile Ser Gly Gly Met Gly Asp Lys Val	260	265	270
Glu Glu Arg Gly Lys Glu Gly Pro Gly Thr Pro Thr Arg Ser Ser Val	275	280	285
Ile Thr Ser Ala Arg Glu Leu His Tyr Gly Arg Glu Glu Ser Ala Glu	290	295	300
Gln Val Pro Pro Pro Ala Glu Ala Gly Gln Ala Pro Thr Gly Arg Pro	305	310	315
			320



170/299

Glu	His	Pro	Ala	Pro	Pro	Pro	Glu	Lys	His	Leu	Gly	Ile	Tyr	Ser	Val	325	330	335
Leu	Pro	Asn	His	Lys	Ala	Asp	Ala	Val	Leu	Ser	Met	Pro	Ser	Ser	Val	340	345	350
Thr	Ser	Gly	Leu	His	Val	Gln	Pro	Ala	Leu	Ala	Val	Ser	Met	Asp	Phe	355	360	365
Ser	Thr	Tyr	Gly	Gly	Leu	Leu	Pro	Gln	Gly	Phe	Ile	Gln	Arg	Glu	Leu	370	375	380
Phe	Ser	Lys	Leu	Gly	Glu	Leu	Ala	Val	Gly	Met	Lys	Ser	Glu	Ser	Arg	385	390	395
Thr	Ile	Gly	Glu	Gln	Cys	Ser	Val	Cys	Gly	Val	Glu	Leu	Pro	Asp	Asn	405	410	415
Glu	Ala	Val	Glu	Gln	His	Arg	Lys	Leu	His	Ser	Gly	Met	Lys	Thr	Tyr	420	425	430
Gly	Cys	Glu	Leu	Cys	Gly	Lys	Arg	Phe	Leu	Asp	Ser	Leu	Arg	Leu	Arg	435	440	445
Met	His	Leu	Leu	Ala	His	Ser	Ala	Gly	Ala	Lys	Ala	Phe	Val	Cys	Asp	450	455	460
Gln	Cys	Gly	Ala	Gln	Phe	Ser	Lys	Glu	Asp	Ala	Leu	Glu	Thr	His	Arg	465	470	475
Gln	Thr	His	Thr	Gly	Thr	Asp	Met	Ala	Val	Phe	Cys	Leu	Leu	Cys	Gly	485	490	495
Lys	Arg	Phe	Gln	Ala	Gln	Ser	Ala	Leu	Gln	Gln	His	Met	Glu	Val	His	500	505	510
Ala	Gly	Val	Arg	Ser	Tyr	Ile	Cys	Ser	Glu	Cys	Asn	Arg	Thr	Phe	Pro	515	520	525
Ser	His	Thr	Ala	Leu	Lys	Arg	His	Leu	Arg	Ser	His	Thr	Gly	Asp	His	530	535	540
Pro	Tyr	Glu	Cys	Glu	Phe	Cys	Gly	Ser	Cys	Phe	Arg	Asp	Glu	Ser	Thr	545	550	555
Leu	Lys	Ser	His	Lys	Arg	Ile	His	Thr	Gly	Glu	Lys	Pro	Tyr	Glu	Cys	565	570	575
Asn	Gly	Cys	Asp	Lys	Lys	Phe	Ser	Leu	Lys	His	Gln	Leu	Glu	Thr	His	580	585	590
Tyr	Arg	Val	His	Thr	Gly	Glu	Lys	Pro	Phe	Glu	Cys	Lys	Leu	Cys	His	595	600	605
Gln	Arg	Ser	Arg	Asp	Tyr	Ser	Ala	Met	Ile	Lys	His	Leu	Arg	Thr	His	610	615	620

171/299

Asn Gly Ala Ser Pro Tyr Gln Cys Thr Ile Cys Thr Glu Tyr Cys Pro  
 625 630 635 640

Ser Leu Ser Ser Met Gln Lys His Met Lys Gly His Lys Pro Glu Glu  
 645 650 655

Ile Pro Pro Asp Trp Arg Ile Glu Lys Thr Tyr Leu Tyr Leu Cys Tyr  
 660 665 670

Val

&lt;210&gt; 215

&lt;211&gt; 2197

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 215

```

caggaagccc acccagcccc gccacgcaga gcccagaagg aaagaaagcc tcatgcctga 60
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caccacacgg ggctactgtg caaggccaac cagatgcggc tggccgggac tttgtgcgat 180
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gaacagtgcc tgaagatgct ggagaccatc caggcctcag acgacaatga cacggaggcc 480
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ggaactcttc agccacctgc agggcccagag gagccaactc tggctggggg tgggcggcac 780
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cacctgcgct cacatacagg cgaccacccc tacgagtgtg agttctgtgg cagctgcttc 1740
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```

&lt;210&gt; 216

172/299

&lt;211&gt; 29

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 216

Arg Glu Phe Glu Asp Arg Asp Arg Ser His Arg Glu Glu Met Glu Glu  
1 5 10 15

Leu Leu Gln Glu Glu Thr Arg Gln Lys Leu Asn Val Ser  
20 25

&lt;210&gt; 217

&lt;211&gt; 89

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 217

acgcgaattt gaagatagag acaggtctca tcgggaggaa atggaggagc tgcttcaaga 60  
agaaaccgg cagaagctca acgtgtcta 89

&lt;210&gt; 218

&lt;211&gt; 26

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 218

Glu Phe Glu Asp Arg Asp Arg Ser His Arg Glu Glu Met Glu Phe Lys  
1 5 10 15

Arg Ala Lys Ala Asn Leu Asp Lys Asn Lys  
20 25

&lt;210&gt; 219

&lt;211&gt; 78

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 219

gaatttgaag atagagacag gtctcatcgg gaggaatgg agttcaagag ggccaaggcg 60  
aacctagaca agaataag 78

&lt;210&gt; 220

&lt;211&gt; 34

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 220

Glu Phe Glu Asp Arg Asp Arg Ser His Arg Glu Glu Met Glu Val His  
1 5 10 15

Glu Leu Glu Lys Ser Lys Arg Ala Leu Glu Thr Gln Met Glu Glu Met  
20 25 30

Lys Thr

173/299

<210> 221  
<211> 102  
<212> DNA  
<213> Homo sapiens

<400> 221  
gaatttgaag atagagacag gtctcatcgg gaggaatgg aggtccatga gctggagaag 60  
tccaagcggg ccctggagac ccagatggag gagatgaaga cg 102

<210> 222  
<211> 50  
<212> PRT  
<213> Homo sapiens

<400> 222  
Glu Phe Glu Asp Arg Asp Arg Ser His Arg Glu Glu Met Glu Asn Glu  
1 5 10 15  
Val Glu Ser Val Thr Gly Met Leu Asn Glu Ala Glu Gly Lys Ala Ile  
20 25 30  
Lys Leu Ala Lys Asp Val Ala Ser Leu Ser Ser Gln Leu Gln Asp Thr  
35 40 45  
Gln Glu  
50

<210> 223  
<211> 152  
<212> DNA  
<213> Homo sapiens

<400> 223  
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acagggatgc ttaacgaggc cgaggggaag gccattaagc tggccaagga cgtggcgtcc 120  
ctcagttccc agctccagga caccaggag tt 152

<210> 224  
<211> 1353  
<212> DNA  
<213> Homo sapiens

<220>  
<221> modified\_base  
<222> (941)  
<223> a, c, t, g, other or unknown

<220>  
<221> modified\_base  
<222> (1067)  
<223> a, c, t, g, other or unknown

<220>

174/299

&lt;221&gt; modified\_base

&lt;222&gt; (1077)

&lt;223&gt; a, c, t, g, other or unknown

&lt;400&gt; 224

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cttggccaac attctggagg cagtaaagaa agcttataga ataaccacat attagaactt 60
gtgaaggaga aaatatacat atatatatat gtatatatat agtctctcta ttaagtaatt 120
taccataagg ggtttaaata ggaatgtttt ctccaaagtg aatcttgaaa tcttggtggt 180
tataattgtc aagcctcttt ttttaaaata gatttgggtca acaggaagta tttttttcta 240
atthtttattt tatagaccta gtcaagcttc ttaattgtta aatattgtta taacaatata 300
tctgggccgg gcgcgggtggc tcactcctgt aatcccagca ctttgggagg ccagggcggg 360
tgaatcacga ggtcaggaga ttgagaccat cctggctaac acaaagaaac cccatctcta 420
ctaaaaatac aaaaaattag ctgggagagg aggagggcgc ctgtagtccc agctactcgg 480
gaggcgggagc ttgcggtgag ccaagatcgc gccactgcac tccagcgact ccgtctcaaa 540
aaaaaaaaaa aaaaaacatc tgagtcggta catggttggt agccgaggag aaaaacatct 600
cttccaaata cgcggtatgag agggacagag ctgaggcaga agccaggagg aaggaaacca 660
aggccctgtc cctggctcgg gcccttgaag aggccttgga agccaaagag gaactcgagc 720
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gcaagaacgt aagtggctct gggtgggttt tctcgtccat gtttcgctg cccaccctct 840
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gaggtgccgc tcacgggtggg tttctcaatc gtcttcatga agttgagcct catagaatgg 1140
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cagatggagg agatgaagac gcagctggaa gagctggagg acgagctgca agccacggag 1260
gacgccaaac tgcggctgga agtcaacatg caggcgctca agggccagtt cgaaagggat 1320
ctccaagccc gggacgagca gaatgaggag aag                                     1353

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&lt;210&gt; 225

&lt;211&gt; 744

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; modified\_base

&lt;222&gt; (326)

&lt;223&gt; a, c, t, g, other or unknown

&lt;220&gt;

&lt;221&gt; modified\_base

&lt;222&gt; (614)

&lt;223&gt; a, c, t, g, other or unknown

&lt;400&gt; 225

```

gcccggctta aaatttagta tcttttagtg attgctagat ctctttgtca gtgagttaat 60
taatctaatt ggctgatagc agctgaggat gtccccaaga atacttgta gctaagagaa 120
gaaaatggag ggatatatgt gatacttggt ttctttgatg ctggttgta tcttggtgatt 180
ttcatatatg tgaatacaag acttccacac catgcccttt ctttcggtat ctgtaaaatt 240
tagaagcttt aaaaatgtata atgtacattt gttacatttc tgaacctttt tgctcatgct 300
ctttgttccc tgatgtagaa tgttcnatc tgtccgtcaa ggcccaacct gaatggtgtc 360
attaaatgtc aggccttttc tcagtctctg ggggtctgaac tgctcagggg tcatcttgag 420
tcccggccat gcatcctgtg ggaggccaaa gccacctccc tgatctcctg aggtgccgct 480
cacggtgggt ttctcaatcg tcttcatgaa gttgagcctc atagaatggg gctgcccgtc 540
ctgccggcag gtccatgagc tggagaagtc caagcgggcc ctggagaccc agatggagga 600
gatgaagacg cagntggaag agctggagga cgagctgcaa gccacggagg acgccaaact 660
gcggctggaa gtcaacatgc aggcgctcaa gggccagttc gaaagggatc tccaagcccc 720

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175/299

ggacgagcag aatgaggaga agag

744

&lt;210&gt; 226

&lt;211&gt; 60

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 226

tctctgtgcc agtagtgggc atgtagagga ccctaataagg agtattcata ccagcagcag 60

&lt;210&gt; 227

&lt;211&gt; 25

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 227

Met	Pro	Arg	Phe	Gly	Phe	Gln	Ile	Gly	Val	Arg	Tyr	Glu	Asn	Lys	Lys
1				5				10					15		

Arg	Glu	Asn	Leu	Ala	Leu	Thr	Leu	Leu
		20				25		

&lt;210&gt; 228

&lt;211&gt; 300

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 228

agctctcctt	gcagcccgag	ctgaccctag	gcctccaccc	tggcaggaat	cccaatttgc	60
ctccacttag	tgagcggaag	aatgtgctac	agttgaaact	ccagcagcgc	cggacccggg	120
aagaactgg	gagccaagg	atcatgccgc	ggtttggttt	tcagatagga	gtaggtatg	180
agaacaagaa	gagagaaaac	ttggcgctga	ccctgttata	gtgggttatag	tggtgtccct	240
aaagggagga	aatgatttca	gcaaaactgg	ttgaacagcg	gatgaagata	tggaattcaa	300

&lt;210&gt; 229

&lt;211&gt; 43

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 229

Lys	Met	Arg	Lys	Met	Glu	Asp	Asn	Gln	Tyr	Ser	Glu	Ala	Glu	Leu	Ser
1				5				10					15		

Ser	Phe	Ser	Thr	Ser	His	Val	Pro	Glu	Glu	Leu	Lys	Gln	Pro	Leu	His
			20				25					30			

Arg	Lys	Ser	Lys	Ser	Gln	Val	Gln	Ile	Phe	Pro
		35				40				

&lt;210&gt; 230

&lt;211&gt; 916

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

176/299

&lt;400&gt; 230

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aaaatgagga aaatggaaga taatcaatat tctgaagctg agctgtcttc ttttagtact 60
tcccatgtgc cagaggaact taagcagccg ttacacagaa agtccaaatc gcaggtagag 120
attttcccat agtacagcat catgggttaca ttatgcatga aacgtacatt tcctttgatt 180
accaaaaaagc aaatattcta tctttgaaat attttagaat ccaaatgggg tcagatgcct 240
ttctaaaaat gttcatatct ttactgtatt tatgaccaa tccaaaatag ttaagcaaga 300
aagcaattaa tttagctgca ttctgtatag aaattttatg acaagcccca tcctacactt 360
atctttcctt gactttgcaa ttctcttact tttgtacagt tagttcatca tgtttgttta 420
caaatattta tgtattacct cagagtcatt ttccgtgtct atactttttg tcaatgtaat 480
tatattttta gatttttctg aaaagtgaat tctatttttt gtccccttct atgtctagta 540
aattgtagg ttagttaa tagcaagtca tctcatgttg taatttaata gtaaaatgag 600
gatcagcaag gaagttagtt gccaaaggtc tacaccaact tactggcaga ttgggaaata 660
aaacctgtca atttaaattc aacaaatgaa tgagtgaatg aatgggtactc aaatttatta 720
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aaatagcaat taaaagagcc tcagtgtttt tgttacaaaa taaaggaagt cgggtactttt 840
ttgtttgaca tccacactca accggattgt tcattcaggt caattaaaaa taaagaaact 900
tcctattacc aaaaaa 916

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&lt;210&gt; 231

&lt;211&gt; 268

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 231

```

Met Phe Arg Met Leu Asn Ser Ser Phe Glu Asp Asp Pro Phe Phe Ser
 1             5             10             15

Glu Ser Ile Leu Ala His Arg Glu Asn Met Arg Gln Met Ile Arg Ser
      20             25             30

Phe Ser Glu Pro Phe Gly Arg Asp Leu Leu Ser Ile Ser Asp Gly Arg
      35             40             45

Gly Arg Ala His Asn Arg Arg Gly His Asn Asp Gly Glu Asp Ser Leu
      50             55             60

Thr His Thr Asp Val Ser Ser Phe Gln Thr Met Asp Gln Met Val Ser
      65             70             75             80

Asn Met Arg Asn Tyr Met Gln Lys Leu Glu Arg Asn Phe Gly Gln Leu
      85             90             95

Ser Val Asp Pro Asn Gly His Ser Phe Cys Ser Ser Ser Val Met Thr
      100             105             110

Tyr Ser Lys Ile Gly Asp Glu Pro Pro Lys Val Phe Gln Ala Ser Thr
      115             120             125

Gln Thr Arg Arg Ala Pro Gly Gly Ile Lys Glu Thr Arg Lys Ala Met
      130             135             140

Arg Asp Ser Asp Ser Gly Leu Glu Lys Met Ala Ile Gly His His Ile
      145             150             155             160

His Asp Arg Ala His Val Ile Lys Lys Ser Lys Asn Lys Lys Thr Gly
      165             170             175

```

Asp	Glu	Glu	Val	Asn	Gln	Glu	Phe	Ile	Asn	Met	Asn	Glu	Ser	Asp	Ala
			180					185					190		
His	Ala	Phe	Asp	Glu	Glu	Trp	Gln	Ser	Glu	Val	Leu	Lys	Tyr	Lys	Pro
		195					200					205			
Gly	Arg	His	Asn	Leu	Gly	Asn	Thr	Arg	Met	Arg	Ser	Val	Gly	His	Glu
	210					215					220				
Asn	Pro	Gly	Ser	Arg	Glu	Leu	Lys	Arg	Arg	Glu	Lys	Pro	Gln	Gln	Ser
225					230					235					240
Pro	Ala	Ile	Glu	His	Gly	Arg	Arg	Ser	Asn	Val	Leu	Gly	Asp	Lys	Leu
				245					250					255	
His	Ile	Lys	Gly	Ser	Ser	Val	Lys	Ser	Asn	Lys	Lys				
			260					265							

<400>	232						
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ctgaacagca	gttttgagga	tgaccccttc	ttctctgagt	ccattcttgc	acaccgagaa	180	
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tctgatggta	gagggagagc	tcataatcgt	agaggacata	atgatggtga	agattctttg	300	
actcatacag	atgtcagctc	tttccagacc	atggaccaaa	tgggtgtcaaa	tatgagaaaac	360	
tatatgcaga	aattgaaaag	aaacttctgg	caactttcag	tggattccaa	tggacattca	420	
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catgtcatta	aaaagtcaaa	gaacaagaag	actggagatg	aagagggtcaa	ccaggagttc	660	
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<400> 233
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 1          5          10          15

Glu Ser Ile Leu Ala His Arg Glu Asn Met Arg Gln Met Ile Arg Ser
          20          25          30

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178/299

Phe Ser Glu Pro Phe Gly Arg Asp Leu Leu Ser Ile Ser Asp Gly Arg  
           35                          40                          45  
 Gly Arg Ala His Asn Arg Arg Gly His Asn Asp Gly Glu Asp Ser Leu  
           50                          55                          60  
 Thr His Thr Asp Val Ser Ser Phe Gln Thr Met Asp Gln Met Val Ser  
           65                          70                          75                          80  
 Asn Met Arg Asn Tyr Met Gln Lys Leu Glu Arg Asn Phe Gly Gln Leu  
                           85                          90                          95  
 Ser Val Asp Pro Asn Gly His Ser Phe Cys Ser Ser Ser Val Met Thr  
                           100                          105                          110  
 Tyr Ser Lys Ile Gly Asp Glu Pro Pro Lys Val Phe Gln Ala Ser Thr  
           115                          120                          125  
 Gln Thr Arg Arg Ala Pro Gly Gly Ile Lys Glu Thr Arg Lys Ala Met  
           130                          135                          140  
 Arg Asp Ser Asp Ser Gly Leu Glu Lys Met Ala Ile Gly His His Ile  
           145                          150                          155                          160  
 His Asp Arg Ala His Val Ile Lys Lys Ser Lys Asn Lys Lys Thr Gly  
                           165                          170                          175  
 Asp Glu Glu Val Asn Gln Glu Phe Ile Asn Met Asn Glu Ser Asp Ala  
                           180                          185                          190  
 His Ala Phe Asp Glu Glu Trp Gln Ser Glu Val Leu Lys Tyr Lys Pro  
           195                          200                          205  
 Gly Arg His Asn Leu Gly Asn Thr Arg Met Arg Ser Val Gly His Glu  
           210                          215                          220  
 Asn Pro Gly Ser Arg Glu Leu Lys Arg Arg Glu Lys Pro Gln Gln Ser  
           225                          230                          235                          240  
 Pro Ala Ile Glu His Gly Arg Arg Ser Asn Val Leu Gly Asp Lys Leu  
                           245                          250                          255  
 His Ile Lys Gly Ser Ser Val Lys Ser Asn Lys Lys  
           260                          265

&lt;210&gt; 234

&lt;211&gt; 1130

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 234

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179/299

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&lt;210&gt; 235

&lt;211&gt; 268

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 235

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Glu Ser Ile Leu Ala His Arg Glu Asn Met Arg Gln Met Ile Arg Ser
      20             25             30

Phe Ser Glu Pro Phe Gly Arg Asp Leu Leu Ser Ile Ser Asp Gly Arg
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Gly Arg Ala His Asn Arg Arg Gly His Asn Asp Gly Glu Asp Ser Leu
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Thr His Thr Asp Val Ser Ser Phe Gln Thr Met Asp Gln Met Val Ser
      65             70             75             80

Asn Met Arg Asn Tyr Met Gln Lys Leu Glu Arg Asn Phe Gly Gln Leu
      85             90             95

Ser Val Asp Pro Asn Gly His Ser Phe Cys Ser Ser Ser Val Met Thr
      100            105            110

Tyr Ser Lys Ile Gly Asp Glu Pro Pro Lys Val Phe Gln Ala Ser Thr
      115            120            125

Gln Thr Arg Arg Ala Pro Gly Gly Ile Lys Glu Thr Arg Lys Ala Met
      130            135            140

Arg Asp Ser Asp Ser Gly Leu Glu Lys Met Ala Ile Gly His His Ile
      145            150            155            160

His Asp Arg Ala His Val Ile Lys Lys Ser Lys Asn Lys Lys Thr Gly
      165            170            175

Asp Glu Glu Val Asn Gln Glu Phe Ile Asn Met Asn Glu Ser Asp Ala
      180            185            190

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180/299

His Ala Phe Asp Glu Glu Trp Gln Ser Glu Val Leu Lys Tyr Lys Pro  
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Gly Arg His Asn Leu Gly Asn Thr Arg Met Arg Ser Val Gly His Glu  
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Asn Pro Gly Ser Arg Glu Leu Lys Arg Arg Glu Lys Pro Gln Gln Ser  
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Pro Ala Ile Glu His Gly Arg Arg Ser Asn Val Leu Gly Asp Lys Leu  
 245 250 255

His Ile Lys Gly Ser Ser Val Lys Ser Asn Lys Lys  
 260 265

&lt;210&gt; 236

&lt;211&gt; 1116

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 236

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&lt;210&gt; 237

&lt;211&gt; 86

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 237

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Asp Arg Glu Lys Gln Pro Ser Glu Gly Ala Phe Ser Glu Asn Asn Ala  
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Glu Asn Glu Ser Gly Gly Asp Lys Pro Pro Ile Asp Pro Asn Asn Pro  
 35 40 45

181/299

Ala Ala Asn Trp Leu His Ala Arg Ser Thr Arg Lys Lys Arg Cys Pro  
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Tyr Thr Lys His Gln Thr Leu Glu Leu Glu Lys Glu Phe Leu Phe Asn  
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Met Tyr Leu Thr Arg Asp  
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 <212> DNA  
 <213> Homo sapiens

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<210> 239  
 <211> 198  
 <212> PRT  
 <213> Homo sapiens

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Arg Arg Arg Ala Arg His Ala Ser Arg Ala Ala Pro Glu Leu Val Gly  
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Asp Leu Gly Ser Phe Leu Leu Leu Gly Ser Thr Phe Leu Ser Thr Gly  
 35 40 45

Thr Thr Leu Pro Phe Ile Thr Ser Val Glu Ile Val Ser Arg Tyr Leu  
 50 55 60

Cys Ala Arg Gly Ser Gly Arg Ala Gly His His Gly Pro Gly Arg Ala  
 65 70 75 80

Arg Pro Ala Val Ala Thr Ser Ala Phe Pro Ala Gln Glu Pro Arg Val  
 85 90 95

Phe Leu Arg Ser Ala Leu Pro Ala Gly Arg Leu Ser Pro Ser Thr Thr  
 100 105 110

His Leu His Leu Val Thr Ala Asp Asn Pro Ala Ala Asn Trp Leu His  
 115 120 125

Ala Arg Ser Thr Arg Lys Lys Arg Cys Pro Tyr Thr Lys His Gln Thr  
 130 135 140

Leu Glu Leu Glu Lys Glu Phe Leu Phe Asn Met Tyr Leu Thr Arg Asp  
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Arg Arg Tyr Glu Val Ala Arg Leu Leu Asn Leu Thr Glu Arg Gln Val  
      165              170          175
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Lys Ile Trp Phe Gln Asn Arg Arg Met Lys Met Lys Lys Ile Asn Lys  
      180              185          190
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Asp Arg Ala Lys Asp Glu  
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			20					25					30			
Asp	Leu	Gly	Ser	Phe	Leu	Leu	Leu	Gly	Ser	Thr	Phe	Leu	Ser	Thr	Gly	
		35					40					45				
Thr	Thr	Leu	Pro	Phe	Ile	Thr	Ser	Val	Glu	Ile	Val	Ser	Arg	Tyr	Leu	
	50					55					60					
Cys	Ala	Arg	Gly	Ser	Gly	Arg	Ala	Gly	His	His	Gly	Pro	Gly	Arg	Ala	
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Arg	Pro	Ala	Val	Ala	Thr	Ser	Ala	Phe	Pro	Ala	Gln	Glu	Pro	Arg	Val	
				85					90					95		
Phe	Leu	Arg	Ser	Ala	Leu	Pro	Ala	Gly	Arg	Leu	Ser	Pro	Ser	Thr	Thr	
			100					105					110			
His	Leu	His	Leu	Val	Thr	Ala	Asp	Asn	Pro	Ala	Ala	Asn	Trp	Leu	His	
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183/299

Ala Arg Ser Thr Arg Lys Lys Arg Cys Pro Tyr Thr Lys His Gln Thr  
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Leu Glu Leu Glu Lys Glu Phe Leu Phe Asn Met Tyr Leu Thr Arg Asp  
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Arg Arg Tyr Glu Val Ala Arg Leu Leu Asn Leu Thr Glu Arg Gln Val  
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Lys Ile Trp Phe Gln Asn Arg Arg Met Lys Met Lys Lys Ile Asn Lys  
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Asp Arg Ala Lys Asp Glu  
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<210> 242  
 <211> 268  
 <212> PRT  
 <213> Homo sapiens

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Gly Ala Asp Ala Ala Asp Glu Leu Ser Val Gly Ala Met Arg Arg Gly  
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 35 40 45

Phe Ser Pro Cys Ser Phe Gln Ser Lys Ala Thr Val Phe Gly Ala Ser  
 50 55 60

Trp Asn Pro Val His Ala Arg Ala Pro Thr Leu Tyr Pro Leu Val Tyr  
 65 70 75 80

His His His His His His Pro Tyr Val His Pro Gln Ala Pro Trp Arg  
 85 90 95

Arg Gly Ala Asp Gly Arg Tyr Met Arg Ser Cys Trp Ser Pro Thr Pro  
 100 105 110

Gly Ala Leu Ser Phe Ala Gly Leu Pro Ser Ser Arg Pro Tyr Gly Ile  
 115 120 125

Lys Pro Glu Pro Leu Ser Ala Arg Arg Gly Asp Cys Pro Thr Leu Asp  
 130 135 140

Thr His Thr Phe Ser Leu Thr Asp Tyr Ala Cys Gly Ser Pro Pro Val  
 145 150 155 160

Asp Arg Glu Lys Gln Pro Ser Glu Gly Ala Phe Ser Glu Asn Asn Ala  
 165 170 175

Glu Asn Glu Ser Gly Gly Asp Lys Pro Pro Ile Asp Pro Asn Asn Pro  
 180 185 190

184/299

Ala Ala Asn Trp Leu His Ala Arg Ser Thr Arg Lys Lys Arg Cys Pro  
 195 200 205

Tyr Thr Lys His Gln Thr Leu Glu Leu Glu Lys Glu Phe Leu Phe Asn  
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Met Tyr Leu Thr Arg Asp Arg Arg Tyr Glu Val Ala Arg Leu Leu Asn  
 225 230 235 240

Leu Thr Glu Arg Gln Val Lys Ile Trp Phe Gln Asn Arg Arg Met Lys  
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Met Lys Lys Ile Asn Lys Asp Arg Ala Lys Asp Glu  
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&lt;210&gt; 243

&lt;211&gt; 6671

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 243

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186/299

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tcaagatctg gttccagaac cgcaggatga aatgaagaa aatcaacaaa gaccgagcaa 6120
aagacgagtg atgccatttg ggcttatatta gaaaaaaggg taagctagag agaaaaagaa 6180
agaactgtcc gtcccccttc cgctttctcc cttttctcac cccacccta gcctccacca 6240
tccccgcaca aagcggtctt aaacctcagg ccacatcttt tccaaggcaa acctgttca 6300
ggctggctcg taggcctgcc gctttgatgg aggaggtatt gtaagctttc attttctata 6360
agaaaaagga aaagttgagg gggggcatta gtgctgatag ctgtgtgtgt tagcttgat 6420
atatattttt aaaaatctac ctgttcctga cttaaaacaa aaggaaagaa actacctttt 6480
tataatgcac aactgttgat ggtaggctgt atagttttta gtctgtgtag ttaatttaat 6540
ttgcagtttg tgcggcagat tgctctgcca agataactga acactgtgtt ttattgtggg 6600
aattatgttt tgtgattcaa acttctgtgt actgggtgat gcaccattg tgattgtgga 6660
agatagaatt c 6671

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&lt;210&gt; 244

&lt;211&gt; 76

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 244

```

Arg Pro Met Pro Arg Leu Glu Pro Thr Phe Glu Ile Asp Glu Glu Glu
 1             5             10             15
Glu Glu Glu Asp Glu Asn Glu Leu Phe Pro Arg Glu Tyr Phe Arg Arg
          20             25             30
Leu Ser Ser Gln Asp Val Leu Arg Cys Gln Ser Ser Ser Lys Arg Lys
          35             40             45
Ser Lys Asp Glu Glu Glu Asp Glu Glu Ser Asp Asp Ala Asp Asp Gly
          50             55             60
Asn Asn Trp Glu His Lys Ser Ile Trp Thr Ala Leu
          65             70             75

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&lt;210&gt; 245

&lt;211&gt; 415

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 245

```

gaggccaatg ccaagattag aaccacatt tgagatcgat gaagaagagg aggaagagga 60
tgaaaatgaa cttttcccta gagaatactt ccgtcgtttg tcttcgcagg atgtactcag 120
gtgtcagtc tcttctaaga ggaagtctaa agatgaagaa gaagatgaag agtcagatga 180
tgctgatgat gggaataact gggaacacaa gtccatttgg acagcccttt agtcaagctg 240
gagggcagcc aatgggagcc actggagtga acccccagtt agccagcaaa cagagcatgg 300
tcaacagttt gccacacctt cctacagata tcaagaatac ttcagtcacc aacgtgccaa 360
atatgtctca gatgcaaaca tcagtgggaa ttgtaccac acaagcaatt gcaac 415

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187/299

&lt;210&gt; 246

&lt;211&gt; 68

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 246

Met Ala Glu Asn Leu Leu Asp Gly Pro Pro Asn Pro Lys Arg Ala Lys  
 1 5 10 15

Leu Ser Ser Pro Gly Phe Ser Ala Asn Asp Ser Thr Asp Thr Pro Ile  
 20 25 30

Leu Lys Pro Val Ser Leu Leu Arg Lys Arg Asp Val Lys Asn Ser Pro  
 35 40 45

Leu Glu Pro Asp Thr Ser Thr Pro Leu Lys Lys Lys Lys Gly Trp Pro  
 50 55 60

Lys Gly Lys Ser  
 65

&lt;210&gt; 247

&lt;211&gt; 229

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 247

gggctgtttt cgcgagcagg tgaaaatggc tgagaacttg ctggacggac cgcccaaccc 60  
 caaaaagagcc aaactcagct cgcccggttt ctcggcgaat gacagcacag acactcctat 120  
 cttaaagcca gtatctcttt tgcgaaaacg tgatgtgaag aattctcctc ttgagccaga 180  
 tacatccaca cttttgaaaa agaaaaaggg atggcccaaa ggcaagagc 229

&lt;210&gt; 248

&lt;211&gt; 376

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 248

Arg Pro Met Pro Arg Leu Glu Pro Thr Phe Glu Ile Asp Glu Glu Glu  
 1 5 10 15

Glu Glu Glu Asp Glu Asn Glu Leu Phe Pro Arg Glu Tyr Phe Arg Arg  
 20 25 30

Leu Ser Ser Gln Asp Val Leu Arg Cys Gln Ser Ser Ser Lys Arg Lys  
 35 40 45

Ser Lys Asp Glu Glu Glu Asp Glu Glu Ser Asp Asp Ala Asp Asp Phe  
 50 55 60

Gly Ser Leu Phe Asp Leu Glu Asn Asp Leu Pro Asp Glu Leu Ile Pro  
 65 70 75 80

Asn Gly Gly Glu Leu Gly Leu Leu Asn Ser Gly Asn Leu Val Pro Asp  
 85 90 95

188/299

Ala Ala Ser Lys His Lys Gln Leu Ser Glu Leu Leu Arg Gly Gly Ser  
 100 105 110  
 Gly Ser Ser Ile Asn Pro Gly Ile Gly Asn Val Ser Ala Ser Ser Pro  
 115 120 125  
 Val Gln Gln Gly Leu Gly Gly Gln Ala Gln Gly Gln Pro Asn Ser Ala  
 130 135 140  
 Asn Met Ala Ser Leu Ser Ala Met Gly Lys Ser Pro Leu Ser Gln Gly  
 145 150 155 160  
 Asp Ser Ser Ala Pro Ser Leu Pro Lys Gln Ala Ala Ser Thr Ser Gly  
 165 170 175  
 Pro Thr Pro Ala Ala Ser Gln Ala Leu Asn Pro Gln Ala Gln Lys Gln  
 180 185 190  
 Val Gly Leu Ala Thr Ser Ser Pro Ala Thr Ser Gln Thr Gly Pro Gly  
 195 200 205  
 Ile Cys Met Asn Ala Asn Phe Asn Gln Thr His Pro Gly Leu Leu Asn  
 210 215 220  
 Ser Asn Ser Gly His Ser Leu Ile Asn Gln Ala Ser Gln Gly Gln Ala  
 225 230 235 240  
 Gln Val Met Asn Gly Ser Leu Gly Ala Ala Gly Arg Gly Arg Gly Ala  
 245 250 255  
 Gly Met Pro Tyr Pro Thr Pro Ala Met Gln Gly Ala Ser Ser Ser Val  
 260 265 270  
 Leu Ala Glu Thr Leu Thr Gln Val Ser Pro Gln Met Thr Gly His Ala  
 275 280 285  
 Gly Leu Asn Thr Ala Gln Ala Gly Gly Met Ala Lys Met Gly Ile Thr  
 290 295 300  
 Gly Asn Thr Ser Pro Phe Gly Gln Pro Phe Ser Gln Ala Gly Gly Gln  
 305 310 315 320  
 Pro Met Gly Ala Thr Gly Val Asn Pro Gln Leu Ala Ser Lys Gln Ser  
 325 330 335  
 Met Val Asn Ser Leu Pro Thr Phe Pro Thr Asp Ile Lys Asn Thr Ser  
 340 345 350  
 Val Thr Asn Val Pro Asn Met Ser Gln Met Gln Thr Ser Val Gly Ile  
 355 360 365  
 Val Pro Thr Gln Ala Ile Ala Thr  
 370 375

<210> 249  
 <211> 1128  
 <212> DNA

189/299

&lt;213&gt; Homo sapiens

&lt;400&gt; 249

```

gaggccaatg ccaagattag aaccacatt tgagatcgat gaagaagagg aggaagagga 60
tgaaaatgaa cttttcccta gagaatactt ccgtcgtttg tcttcgcagg atgtactcag 120
gtgtcagtc tcttctaaga ggaagtctaa agatgaagaa gaagatgaag agtcagatga 180
tgctgatgat tttggatcat tgtttgactt ggaaaatgat cttcctgatg agctgatacc 240
caatggagga gaattaggcc ttttaaacag tgggaacctt gttccagatg ctgcttccaa 300
acataaacia ctgtcggagc ttctacgagg aggcagcggc tctagtatca acccaggaat 360
aggaaatgtg agcgccagca gcccctgca gcagggcctg ggtggccagg ctcaagggca 420
gccgaacagt gctaactagg ccagcctcag tgccatgggc aagagccctc tgagccaggg 480
agattcttca gccccagcc tgcctaaaca ggcagccagc acctctgggc ccaccccgcc 540
tgctcccaa gcaactgaat cgcaagcaca aaagcaagtg gggctggcga ctagcagccc 600
tgccacgtca cagactggac ctggtatctg catgaatgct aactttaacc agaccaccc 660
aggcctctc aatagtaact ctggccatag cttaattaat caggcttcac aagggcaggc 720
gcaagtcatg aatggatctc ttggggctgc tggcagagga aggggagctg gaatgccgta 780
ccctactcca gccatgcagg gcgcctcgag cagcgtgctg gctgagaccc taacgcaggt 840
ttccccgcaa atgactggtc acgcgggact gaacaccgca caggcaggag gcatggccaa 900
gatgggaata actgggaaca caagtccatt tggacagccc tttagtcaag ctggagggca 960
gccaatggga gccactggag tgaaccccca gttagccagc aaacagagca tggtaacag 1020
tttgcaccac ttccctacag atatcaagaa tacttcagtc accaacgtgc caaatatgtc 1080
tcagatgcaa acatcagtgg gaattgtacc cacacaagca attgcaac 1128

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&lt;210&gt; 250

&lt;211&gt; 2004

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 250

```

Met Val Lys Leu Ala Asn Pro Leu Tyr Thr Glu Trp Ile Leu Glu Ala
  1              5              10              15

Ile Lys Lys Val Lys Lys Gln Lys Gln Arg Pro Ser Glu Glu Arg Ile
      20              25              30

Cys Asn Ala Val Ser Ser Ser His Gly Leu Asp Arg Lys Thr Val Leu
      35              40              45

Glu Gln Leu Glu Leu Ser Val Lys Asp Gly Thr Ile Leu Lys Val Ser
      50              55              60

Asn Lys Gly Leu Asn Ser Tyr Lys Asp Pro Asp Asn Pro Gly Arg Ile
      65              70              75              80

Ala Leu Pro Lys Pro Arg Asn His Gly Lys Leu Asp Asn Lys Gln Asn
      85              90              95

Val Asp Trp Asn Lys Leu Ile Lys Arg Ala Val Glu Gly Leu Ala Glu
      100             105             110

Ser Gly Gly Ser Thr Leu Lys Ser Ile Glu Arg Phe Leu Lys Gly Gln
      115             120             125

Lys Asp Val Ser Ala Leu Phe Gly Gly Ser Ala Ala Ser Gly Phe His
      130             135             140

Gln Gln Leu Arg Leu Ala Ile Lys Arg Ala Ile Gly His Gly Arg Leu

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190/299

145		150		155		160
Leu Lys Asp Gly Pro	Leu Tyr Arg Leu Asn Thr Lys Ala Thr Asn Val					
	165		170			175
Asp Gly Lys Glu Ser Cys Glu Ser	Leu Ser Cys Leu Pro Pro Val Ser					
	180		185			190
Leu Leu Pro His Glu Lys Asp Lys	Pro Val Ala Glu Pro Ile Pro Ile					
	195		200			205
Cys Ser Phe Cys Leu Gly Thr Lys Glu Gln Asn Arg Glu Lys Lys Pro						
	210		215			220
Glu Glu Leu Ile Ser Cys Ala Asp Cys Gly Asn Ser Gly His Pro Ser						
	225		230			235
Cys Leu Lys Phe Ser Pro Glu Leu Thr Val Arg Val Lys Ala Leu Arg						
	245		250			255
Trp Gln Cys Ile Glu Cys Lys Thr Cys Ser Ser Cys Arg Asp Gln Gly						
	260		265			270
Lys Asn Ala Asp Asn Met Leu Phe Cys Asp Ser Cys Asp Arg Gly Phe						
	275		280			285
His Met Glu Cys Cys Asp Pro Pro Leu Thr Arg Met Pro Lys Gly Met						
	290		295			300
Trp Ile Cys Gln Ile Cys Arg Pro Arg Lys Lys Gly Arg Lys Leu Leu						
	305		310			315
Gln Lys Lys Ala Ala Gln Ile Lys Arg Arg Tyr Thr Asn Pro Ile Gly						
	325		330			335
Arg Pro Lys Asn Arg Leu Lys Lys Gln Asn Thr Val Ser Lys Gly Pro						
	340		345			350
Phe Ser Lys Val Arg Thr Gly Pro Gly Arg Gly Arg Lys Arg Lys Ile						
	355		360			365
Thr Leu Ser Ser Gln Ser Ala Ser Ser Ser Ser Glu Glu Gly Tyr Leu						
	370		375			380
Glu Arg Ile Asp Gly Leu Asp Phe Cys Arg Asp Ser Asn Val Ser Leu						
	385		390			395
Arg Phe Asn Lys Lys Thr Lys Gly Leu Ile Asp Gly Leu Thr Lys Phe						
	405		410			415
Phe Thr Pro Ser Pro Asp Gly Arg Lys Ala Arg Gly Glu Val Val Asp						
	420		425			430
Tyr Ser Glu Gln Tyr Arg Ile Arg Lys Arg Gly Asn Arg Lys Ser Ser						
	435		440			445
Thr Ser Asp Trp Pro Thr Asp Asn Gln Asp Gly Trp Asp Gly Lys Gln						
	450		455			460

191/299

Glu	Asn	Glu	Glu	Arg	Leu	Phe	Gly	Ser	Gln	Glu	Ile	Met	Thr	Glu	Lys	465	470	475	480
Asp	Met	Glu	Leu	Phe	Arg	Asp	Ile	Gln	Glu	Gln	Ala	Leu	Gln	Lys	Val	485	490	495	
Gly	Val	Thr	Gly	Pro	Pro	Asp	Pro	Gln	Val	Arg	Cys	Pro	Ser	Val	Ile	500	505	510	
Glu	Phe	Gly	Lys	Tyr	Glu	Ile	His	Thr	Trp	Tyr	Ser	Ser	Pro	Tyr	Pro	515	520	525	
Gln	Glu	Tyr	Ser	Arg	Leu	Pro	Lys	Leu	Tyr	Leu	Cys	Glu	Phe	Cys	Leu	530	535	540	
Lys	Tyr	Met	Lys	Ser	Arg	Thr	Ile	Leu	Gln	Gln	His	Met	Lys	Lys	Cys	545	550	555	560
Gly	Trp	Phe	His	Pro	Pro	Ala	Asn	Glu	Ile	Tyr	Arg	Lys	Asn	Asn	Ile	565	570	575	
Ser	Val	Phe	Glu	Val	Asp	Gly	Asn	Val	Ser	Thr	Ile	Tyr	Cys	Gln	Asn	580	585	590	
Leu	Cys	Leu	Leu	Ala	Lys	Leu	Phe	Leu	Asp	His	Lys	Thr	Leu	Tyr	Tyr	595	600	605	
Asp	Val	Glu	Pro	Phe	Leu	Phe	Tyr	Val	Leu	Thr	Gln	Asn	Asp	Val	Lys	610	615	620	
Gly	Cys	His	Leu	Val	Gly	Tyr	Phe	Ser	Lys	Glu	Lys	His	Cys	Gln	Gln	625	630	635	640
Lys	Tyr	Asn	Val	Ser	Cys	Ile	Met	Ile	Leu	Pro	Gln	Tyr	Gln	Arg	Lys	645	650	655	
Gly	Tyr	Gly	Arg	Phe	Leu	Ile	Asp	Phe	Ser	Tyr	Leu	Leu	Ser	Lys	Arg	660	665	670	
Glu	Gly	Gln	Ala	Gly	Ser	Pro	Glu	Lys	Pro	Leu	Ser	Asp	Leu	Gly	Arg	675	680	685	
Leu	Ser	Tyr	Met	Ala	Tyr	Trp	Lys	Ser	Val	Ile	Leu	Glu	Cys	Leu	Tyr	690	695	700	
His	Gln	Asn	Asp	Lys	Gln	Ile	Ser	Ile	Lys	Lys	Leu	Ser	Lys	Leu	Thr	705	710	715	720
Gly	Ile	Cys	Pro	Gln	Asp	Ile	Thr	Ser	Thr	Leu	His	His	Leu	Arg	Met	725	730	735	
Leu	Asp	Phe	Arg	Ser	Asp	Gln	Phe	Val	Ile	Ile	Arg	Arg	Glu	Lys	Leu	740	745	750	
Ile	Gln	Asp	His	Met	Ala	Lys	Leu	Gln	Leu	Asn	Leu	Arg	Pro	Val	Asp	755	760	765	

192/299

Val	Asp	Pro	Glu	Cys	Leu	Arg	Trp	Thr	Pro	Val	Ile	Val	Ser	Asn	Ser	770	775	780
Val	Val	Ser	Glu	Glu	Glu	Glu	Glu	Glu	Ala	Glu	Glu	Gly	Glu	Asn	Glu	785	790	795
Glu	Pro	Gln	Cys	Gln	Glu	Arg	Glu	Leu	Glu	Ile	Ser	Val	Gly	Lys	Ser	805	810	815
Val	Ser	His	Glu	Asn	Lys	Glu	Gln	Asp	Ser	Tyr	Ser	Val	Glu	Ser	Glu	820	825	830
Lys	Lys	Pro	Glu	Val	Met	Ala	Pro	Val	Ser	Ser	Thr	Arg	Leu	Ser	Lys	835	840	845
Gln	Val	Leu	Pro	His	Asp	Ser	Leu	Pro	Ala	Asn	Ser	Gln	Pro	Ser	Arg	850	855	860
Arg	Gly	Arg	Trp	Gly	Arg	Lys	Asn	Arg	Lys	Thr	Gln	Glu	Arg	Phe	Gly	865	870	875
Asp	Lys	Asp	Ser	Lys	Leu	Leu	Leu	Glu	Glu	Thr	Ser	Ser	Ala	Pro	Gln	885	890	895
Glu	Gln	Tyr	Gly	Glu	Cys	Gly	Glu	Lys	Ser	Glu	Ala	Thr	Gln	Glu	Gln	900	905	910
Tyr	Thr	Glu	Ser	Glu	Glu	Gln	Leu	Val	Ala	Ser	Glu	Glu	Gln	Pro	Ser	915	920	925
Gln	Asp	Gly	Lys	Pro	Asp	Leu	Pro	Lys	Arg	Arg	Leu	Ser	Glu	Gly	Val	930	935	940
Glu	Pro	Trp	Arg	Gly	Gln	Leu	Lys	Lys	Ser	Pro	Glu	Ala	Leu	Lys	Cys	945	950	955
Arg	Leu	Thr	Glu	Gly	Ser	Glu	Arg	Leu	Pro	Arg	Arg	Tyr	Ser	Glu	Gly	965	970	975
Asp	Arg	Ala	Val	Leu	Arg	Gly	Phe	Ser	Glu	Ser	Ser	Glu	Glu	Glu	Glu	980	985	990
Glu	Pro	Glu	Ser	Pro	Arg	Ser	Ser	Ser	Pro	Pro	Ile	Leu	Thr	Lys	Pro	995	1000	1005
Thr	Leu	Lys	Arg	Lys	Lys	Pro	Phe	Leu	His	Arg	Arg	Arg	Arg	Val	Arg	1010	1015	1020
Lys	Arg	Lys	His	His	Asn	Ser	Ser	Val	Val	Thr	Glu	Thr	Ile	Ser	Glu	1025	1030	1035
Thr	Thr	Glu	Val	Leu	Asp	Glu	Pro	Phe	Glu	Asp	Ser	Asp	Ser	Glu	Arg	1045	1050	1055
Pro	Met	Pro	Arg	Leu	Glu	Pro	Thr	Phe	Glu	Ile	Asp	Glu	Glu	Glu	Glu	1060	1065	1070
Glu	Glu	Asp	Glu	Asn	Glu	Leu	Phe	Pro	Arg	Glu	Tyr	Phe	Arg	Arg	Leu			

193/299

1075	1080	1085
Ser Ser Gln Asp Val Leu Arg Cys Gln Ser Ser Ser Lys Arg Lys Ser 1090	1095	1100
Lys Asp Glu Glu Glu Asp Glu Glu Ser Asp Asp Ala Asp Asp Thr Pro 1105	1110	1115 1120
Ile Leu Lys Pro Val Ser Leu Leu Arg Lys Arg Asp Val Lys Asn Ser 1125	1130	1135
Pro Leu Glu Pro Asp Thr Ser Thr Pro Leu Lys Lys Lys Lys Gly Trp 1140	1145	1150
Pro Lys Gly Lys Ser Arg Lys Pro Ile His Trp Lys Lys Arg Pro Gly 1155	1160	1165
Arg Lys Pro Gly Phe Lys Leu Ser Arg Glu Ile Met Pro Val Ser Thr 1170	1175	1180
Gln Ala Cys Val Ile Glu Pro Ile Val Ser Ile Pro Lys Ala Gly Arg 1185	1190	1195 1200
Lys Pro Lys Ile Gln Glu Ser Glu Glu Thr Val Glu Pro Lys Glu Asp 1205	1210	1215
Met Pro Leu Pro Glu Glu Arg Lys Glu Glu Glu Glu Met Gln Ala Glu 1220	1225	1230
Ala Glu Glu Ala Glu Glu Gly Glu Glu Glu Asp Ala Ala Ser Ser Glu 1235	1240	1245
Val Pro Ala Ala Ser Pro Ala Asp Ser Ser Asn Ser Pro Glu Thr Glu 1250	1255	1260
Thr Lys Glu Pro Glu Val Glu Glu Glu Glu Glu Lys Pro Arg Val Ser 1265	1270	1275 1280
Glu Glu Gln Arg Gln Ser Glu Glu Glu Gln Gln Glu Leu Glu Glu Pro 1285	1290	1295
Glu Pro Glu Glu Glu Glu Asp Ala Ala Ala Glu Thr Ala Gln Asn Asp 1300	1305	1310
Asp His Asp Ala Asp Asp Glu Asp Asp Gly His Leu Glu Ser Thr Lys 1315	1320	1325
Lys Lys Glu Leu Glu Glu Gln Pro Thr Arg Glu Asp Val Lys Glu Glu 1330	1335	1340
Pro Gly Val Gln Glu Ser Phe Leu Asp Ala Asn Met Gln Lys Ser Arg 1345	1350	1355 1360
Glu Lys Ile Lys Asp Lys Glu Glu Thr Glu Leu Asp Ser Glu Glu Glu 1365	1370	1375
Gln Pro Ser His Asp Thr Ser Val Val Ser Glu Gln Met Ala Gly Ser 1380	1385	1390



194/299

Glu Asp Asp His Glu Glu Asp Ser His Thr Lys Glu Glu Leu Ile Glu  
1395 1400 1405

Leu Lys Glu Glu Glu Glu Ile Pro His Ser Glu Leu Asp Leu Glu Thr  
1410 1415 1420

Val Gln Ala Val Gln Ser Leu Thr Gln Glu Glu Ser Ser Glu His Glu  
1425 1430 1435 1440

Gly Ala Tyr Gln Asp Cys Glu Glu Thr Leu Ala Ala Cys Gln Thr Leu  
1445 1450 1455

Gln Ser Tyr Thr Gln Ala Asp Glu Asp Pro Gln Met Ser Met Val Glu  
1460 1465 1470

Asp Cys His Ala Ser Glu His Asn Ser Pro Ile Ser Ser Val Gln Ser  
1475 1480 1485

His Pro Ser Gln Ser Val Arg Ser Val Ser Ser Pro Asn Val Pro Ala  
1490 1495 1500

Leu Glu Ser Gly Tyr Thr Gln Ile Ser Pro Glu Gln Gly Ser Leu Ser  
1505 1510 1515 1520

Ala Pro Ser Met Gln Asn Met Glu Thr Ser Pro Met Met Asp Val Pro  
1525 1530 1535

Ser Val Ser Asp His Ser Gln Gln Val Val Asp Ser Gly Phe Ser Asp  
1540 1545 1550

Leu Gly Ser Ile Glu Ser Thr Thr Glu Asn Tyr Glu Asn Pro Ser Ser  
1555 1560 1565

Tyr Asp Ser Thr Met Gly Gly Ser Ile Cys Gly Asn Ser Ser Ser Gln  
1570 1575 1580

Ser Ser Cys Ser Tyr Gly Gly Leu Ser Ser Ser Ser Ser Leu Thr Gln  
1585 1590 1595 1600

Ser Ser Cys Val Val Thr Gln Gln Met Ala Ser Met Gly Ser Ser Cys  
1605 1610 1615

Ser Met Met Gln Gln Ser Ser Val Gln Pro Ala Ala Asn Cys Ser Ile  
1620 1625 1630

Lys Ser Pro Gln Ser Cys Val Val Glu Arg Pro Pro Ser Asn Gln Gln  
1635 1640 1645

Gln Gln Pro Pro Pro Pro Pro Pro Gln Gln Pro Gln Pro Pro Pro Pro  
1650 1655 1660

Gln Pro Gln Pro Ala Pro Gln Pro Pro Pro Pro Gln Gln Gln Pro Gln  
1665 1670 1675 1680

Gln Gln Pro Gln Pro Gln Pro Gln Gln Pro Pro Pro Pro Pro Pro Pro  
1685 1690 1695

195/299

Gln Gln Gln Pro Pro Leu Ser Gln Cys Ser Met Asn Asn Ser Phe Thr  
 1700 1705 1710  
 Pro Ala Pro Met Ile Met Glu Ile Pro Glu Ser Gly Ser Thr Gly Asn  
 1715 1720 1725  
 Ile Ser Ile Tyr Glu Arg Ile Pro Gly Asp Phe Gly Ala Gly Ser Tyr  
 1730 1735 1740  
 Ser Gln Pro Ser Ala Thr Phe Ser Leu Ala Lys Leu Gln Gln Leu Thr  
 1745 1750 1755 1760  
 Asn Thr Ile Met Asp Pro His Ala Met Pro Tyr Ser His Ser Pro Ala  
 1765 1770 1775  
 Val Thr Ser Tyr Ala Thr Ser Val Ser Leu Ser Asn Thr Gly Leu Ala  
 1780 1785 1790  
 Gln Leu Ala Pro Ser His Pro Leu Ala Gly Thr Pro Gln Ala Gln Ala  
 1795 1800 1805  
 Thr Met Thr Pro Pro Pro Asn Leu Ala Ser Thr Thr Met Asn Leu Thr  
 1810 1815 1820  
 Ser Pro Leu Leu Gln Cys Asn Met Ser Ala Thr Asn Ile Gly Ile Pro  
 1825 1830 1835 1840  
 His Thr Gln Arg Leu Gln Gly Gln Met Pro Val Lys Gly His Ile Ser  
 1845 1850 1855  
 Ile Arg Ser Lys Ser Ala Pro Leu Pro Ser Ala Ala Ala His Gln Gln  
 1860 1865 1870  
 Gln Leu Tyr Gly Arg Ser Pro Ser Ala Val Ala Met Gln Ala Gly Pro  
 1875 1880 1885  
 Arg Ala Leu Ala Val Gln Arg Gly Met Asn Met Gly Val Asn Leu Met  
 1890 1895 1900  
 Pro Thr Pro Ala Tyr Asn Val Asn Ser Met Asn Met Asn Thr Leu Asn  
 1905 1910 1915 1920  
 Ala Met Asn Ser Tyr Arg Met Thr Gln Pro Met Met Asn Ser Ser Tyr  
 1925 1930 1935  
 His Ser Asn Pro Ala Tyr Met Asn Gln Thr Ala Gln Tyr Pro Met Gln  
 1940 1945 1950  
 Met Gln Met Gly Met Met Gly Ser Gln Ala Tyr Thr Gln Gln Pro Met  
 1955 1960 1965  
 Gln Pro Asn Pro His Gly Asn Met Met Tyr Thr Gly Pro Ser His His  
 1970 1975 1980  
 Ser Tyr Met Asn Ala Ala Gly Val Pro Lys Gln Ser Leu Asn Gly Pro  
 1985 1990 1995 2000  
 Tyr Met Arg Arg

<210> 251  
<211> 7869  
<212> DNA  
<213> Homo sapiens

<400> 251

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ttcttacaac	tttatgacga	gacccatgtg	tggtgctatt	gagaaattca	ttgggaagtt	180
ggaagacatt	tcaaacaca	ggttggtttg	gtttctatag	tacaattggg	gtggcattct	240
gttttgtgaa	aggaggaagg	acttaggcca	gaaaactcat	atgctatggg	taactgggtc	300
ccagcctccg	agaatcttgt	tttccatggg	gtaaaaactta	ctcagcatca	ggataaggga	360
taacgactct	atggatatac	agaatccttc	accatggtaa	aactcgcaaa	cccgctttat	420
actgagtggg	ttttggaggc	catcaaaaaa	gtgaaaaagc	agaaacagcg	tccttcagaa	480
gaaaggatat	gcaatgctgt	gtcttcatcc	catggcttgg	atcgtaaaac	tgtttttagaa	540
caattggagt	tgagtgttaa	agatggaaca	attttaaaaag	tctcaaataa	aggactcaat	600
tcctataaag	atcctgataa	tcctgggcca	atagcacttc	ctaagcctcg	gaacccatgga	660
aaattggata	ataaacaaaa	tgtggattgg	aataaactga	taaagcgggc	agttgagggc	720
ttggcagagt	ctgggtggctc	aactttgaaa	agcattgaac	gttttttgaa	aggtcagaag	780
gatgtgtctg	cattattccg	aggcagtgtc	gcctctggct	ttcaccagca	gttacgattg	840
gctatcaaac	gtgccattgg	ccacggcaga	ctccttaaaag	atggacctct	ttatcggtc	900
aacactaaag	caaccaacgt	ggatgggaaa	gagagtgtgt	agtctctttc	ctgtttacct	960
ccagtgtccc	ttcttccaca	tgaaaaggat	aagccggttg	ctgaaccaat	ccccatctgt	1020
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198/299

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aaaaaaaaa

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&lt;210&gt; 252

&lt;211&gt; 2442

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 252

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Met Ala Glu Asn Leu Leu Asp Gly Pro Pro Asn Pro Lys Arg Ala Lys
  1                      5                      10                     15

Leu Ser Ser Pro Gly Phe Ser Ala Asn Asp Ser Thr Asp Phe Gly Ser
          20                     25                     30

Leu Phe Asp Leu Glu Asn Asp Leu Pro Asp Glu Leu Ile Pro Asn Gly
      35                      40                      45

Gly Glu Leu Gly Leu Leu Asn Ser Gly Asn Leu Val Pro Asp Ala Ala
      50                      55                      60

Ser Lys His Lys Gln Leu Ser Glu Leu Leu Arg Gly Gly Ser Gly Ser
      65                      70                      75                     80

Ser Ile Asn Pro Gly Ile Gly Asn Val Ser Ala Ser Ser Pro Val Gln
          85                     90                     95

Gln Gly Leu Gly Gly Gln Ala Gln Gly Gln Pro Asn Ser Ala Asn Met
      100                     105                     110

Ala Ser Leu Ser Ala Met Gly Lys Ser Pro Leu Ser Gln Gly Asp Ser
      115                     120                     125

Ser Ala Pro Ser Leu Pro Lys Gln Ala Ala Ser Thr Ser Gly Pro Thr
      130                     135                     140

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199/299

Pro Ala Ala Ser Gln Ala Leu Asn Pro Gln Ala Gln Lys Gln Val Gly  
 145 150 155 160  
 Leu Ala Thr Ser Ser Pro Ala Thr Ser Gln Thr Gly Pro Gly Ile Cys  
 165 170 175  
 Met Asn Ala Asn Phe Asn Gln Thr His Pro Gly Leu Leu Asn Ser Asn  
 180 185 190  
 Ser Gly His Ser Leu Ile Asn Gln Ala Ser Gln Gly Gln Ala Gln Val  
 195 200 205  
 Met Asn Gly Ser Leu Gly Ala Ala Gly Arg Gly Arg Gly Ala Gly Met  
 210 215 220  
 Pro Tyr Pro Thr Pro Ala Met Gln Gly Ala Ser Ser Ser Val Leu Ala  
 225 230 235 240  
 Glu Thr Leu Thr Gln Val Ser Pro Gln Met Thr Gly His Ala Gly Leu  
 245 250 255  
 Asn Thr Ala Gln Ala Gly Gly Met Ala Lys Met Gly Ile Thr Gly Asn  
 260 265 270  
 Thr Ser Pro Phe Gly Gln Pro Phe Ser Gln Ala Gly Gly Gln Pro Met  
 275 280 285  
 Gly Ala Thr Gly Val Asn Pro Gln Leu Ala Ser Lys Gln Ser Met Val  
 290 295 300  
 Asn Ser Leu Pro Thr Phe Pro Thr Asp Ile Lys Asn Thr Ser Val Thr  
 305 310 315 320  
 Asn Val Pro Asn Met Ser Gln Met Gln Thr Ser Val Gly Ile Val Pro  
 325 330 335  
 Thr Gln Ala Ile Ala Thr Gly Pro Thr Ala Asp Pro Glu Lys Arg Lys  
 340 345 350  
 Leu Ile Gln Gln Gln Leu Val Leu Leu Leu His Ala His Lys Cys Gln  
 355 360 365  
 Arg Arg Glu Gln Ala Asn Gly Glu Val Arg Ala Cys Ser Leu Pro His  
 370 375 380  
 Cys Arg Thr Met Lys Asn Val Leu Asn His Met Thr His Cys Gln Ala  
 385 390 395 400  
 Gly Lys Ala Cys Gln Val Ala His Cys Ala Ser Ser Arg Gln Ile Ile  
 405 410 415  
 Ser His Trp Lys Asn Cys Thr Arg His Asp Cys Pro Val Cys Leu Pro  
 420 425 430  
 Leu Lys Asn Ala Ser Asp Lys Arg Asn Gln Gln Thr Ile Leu Gly Ser  
 435 440 445

200/299

Pro Ala Ser Gly Ile Gln Asn Thr Ile Gly Ser Val Gly Thr Gly Gln  
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 Met Gln Arg Ala Tyr Ala Ala Leu Gly Leu Pro Tyr Met Asn Gln Pro  
 485 490 495  
 Gln Thr Gln Leu Gln Pro Gln Val Pro Gly Gln Gln Pro Ala Gln Pro  
 500 505 510  
 Gln Thr His Gln Gln Met Arg Thr Leu Asn Pro Leu Gly Asn Asn Pro  
 515 520 525  
 Met Asn Ile Pro Ala Gly Gly Ile Thr Thr Asp Gln Gln Pro Pro Asn  
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 Leu Ile Ser Glu Ser Ala Leu Pro Thr Ser Leu Gly Ala Thr Asn Pro  
 545 550 555 560  
 Leu Met Asn Asp Gly Ser Asn Ser Gly Asn Ile Gly Thr Leu Ser Thr  
 565 570 575  
 Ile Pro Thr Ala Ala Pro Pro Ser Ser Thr Gly Val Arg Lys Gly Trp  
 580 585 590  
 His Glu His Val Thr Gln Asp Leu Arg Ser His Leu Val His Lys Leu  
 595 600 605  
 Val Gln Ala Ile Phe Pro Thr Pro Asp Pro Ala Ala Leu Lys Asp Arg  
 610 615 620  
 Arg Met Glu Asn Leu Val Ala Tyr Ala Lys Lys Val Glu Gly Asp Met  
 625 630 635 640  
 Tyr Glu Ser Ala Asn Ser Arg Asp Glu Tyr Tyr His Leu Leu Ala Glu  
 645 650 655  
 Lys Ile Tyr Lys Ile Gln Lys Glu Leu Glu Glu Lys Arg Arg Ser Arg  
 660 665 670  
 Leu His Lys Gln Gly Ile Leu Gly Asn Gln Pro Ala Leu Pro Ala Pro  
 675 680 685  
 Gly Ala Gln Pro Pro Val Ile Pro Gln Ala Gln Pro Val Arg Pro Pro  
 690 695 700  
 Asn Gly Pro Leu Ser Leu Pro Val Asn Arg Met Gln Val Ser Gln Gly  
 705 710 715 720  
 Met Asn Ser Phe Asn Pro Met Ser Leu Gly Asn Val Gln Leu Pro Gln  
 725 730 735  
 Ala Pro Met Gly Pro Arg Ala Ala Ser Pro Met Asn His Ser Val Gln  
 740 745 750  
 Met Asn Ser Met Gly Ser Val Pro Gly Met Ala Ile Ser Pro Ser Arg

201/299

755					760					765					
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770						775					780				
Ala	Gln	Ala	Pro	Ala	Gln	Ser	Gln	Phe	Leu	Pro	Gln	Asn	Gln	Phe	Pro
785					790					795					800
Ser	Ser	Ser	Gly	Ala	Met	Ser	Val	Gly	Met	Gly	Gln	Pro	Pro	Ala	Gln
				805					810					815	
Thr	Gly	Val	Ser	Gln	Gly	Gln	Val	Pro	Gly	Ala	Ala	Leu	Pro	Asn	Pro
			820					825					830		
Leu	Asn	Met	Leu	Gly	Pro	Gln	Ala	Ser	Gln	Leu	Pro	Cys	Pro	Pro	Val
		835					840					845			
Thr	Gln	Ser	Pro	Leu	His	Pro	Thr	Pro	Pro	Pro	Ala	Ser	Thr	Ala	Ala
		850				855					860				
Gly	Met	Pro	Ser	Leu	Gln	His	Thr	Thr	Pro	Pro	Gly	Met	Thr	Pro	Pro
865					870					875					880
Gln	Pro	Ala	Ala	Pro	Thr	Gln	Pro	Ser	Thr	Pro	Val	Ser	Ser	Ser	Gly
				885					890					895	
Gln	Thr	Pro	Thr	Pro	Thr	Pro	Gly	Ser	Val	Pro	Ser	Ala	Thr	Gln	Thr
			900					905					910		
Gln	Ser	Thr	Pro	Thr	Val	Gln	Ala	Ala	Ala	Gln	Ala	Gln	Val	Thr	Pro
		915					920					925			
Gln	Pro	Gln	Thr	Pro	Val	Gln	Pro	Pro	Ser	Val	Ala	Thr	Pro	Gln	Ser
		930				935					940				
Ser	Gln	Gln	Gln	Pro	Thr	Pro	Val	His	Ala	Gln	Pro	Pro	Gly	Thr	Pro
945					950					955					960
Leu	Ser	Gln	Ala	Ala	Ala	Ser	Ile	Asp	Asn	Arg	Val	Pro	Thr	Pro	Ser
				965					970					975	
Ser	Val	Ala	Ser	Ala	Glu	Thr	Asn	Ser	Gln	Gln	Pro	Gly	Pro	Asp	Val
			980					985					990		
Pro	Val	Leu	Glu	Met	Lys	Thr	Glu	Thr	Gln	Ala	Glu	Asp	Thr	Glu	Pro
		995				1000						1005			
Asp	Pro	Gly	Glu	Ser	Lys	Gly	Glu	Pro	Arg	Ser	Glu	Met	Met	Glu	Glu
1010						1015					1020				
Asp	Leu	Gln	Gly	Ala	Ser	Gln	Val	Lys	Glu	Glu	Thr	Asp	Ile	Ala	Glu
1025					1030					1035					1040
Gln	Lys	Ser	Glu	Pro	Met	Glu	Val	Asp	Glu	Lys	Lys	Pro	Glu	Val	Lys
				1045				1050						1055	
Val	Glu	Val	Lys	Glu	Glu	Glu	Glu	Ser	Ser	Ser	Asn	Gly	Thr	Ala	Ser
			1060					1065					1070		



202/299

Gln Ser Thr Ser Pro Ser Gln Pro Arg Lys Lys Ile Phe Lys Pro Glu  
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 Glu Leu Arg Gln Ala Leu Met Pro Thr Leu Glu Ala Leu Tyr Arg Gln  
 1090 1095 1100  
 Asp Pro Glu Ser Leu Pro Phe Arg Gln Pro Val Asp Pro Gln Leu Leu  
 1105 1110 1115 1120  
 Gly Ile Pro Asp Tyr Phe Asp Ile Val Lys Asn Pro Met Asp Leu Ser  
 1125 1130 1135  
 Thr Ile Lys Arg Lys Leu Asp Thr Gly Gln Tyr Gln Glu Pro Trp Gln  
 1140 1145 1150  
 Tyr Val Asp Asp Val Trp Leu Met Phe Asn Asn Ala Trp Leu Tyr Asn  
 1155 1160 1165  
 Arg Lys Thr Ser Arg Val Tyr Lys Phe Cys Ser Lys Leu Ala Glu Val  
 1170 1175 1180  
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 1185 1190 1195 1200  
 Gly Arg Lys Tyr Glu Phe Ser Pro Gln Thr Leu Cys Cys Tyr Gly Lys  
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 Gln Leu Cys Thr Ile Pro Arg Asp Ala Ala Tyr Tyr Ser Tyr Gln Asn  
 1220 1225 1230  
 Arg Tyr His Phe Cys Glu Lys Cys Phe Thr Glu Ile Gln Gly Glu Asn  
 1235 1240 1245  
 Val Thr Leu Gly Asp Asp Pro Ser Gln Pro Gln Thr Thr Ile Ser Lys  
 1250 1255 1260  
 Asp Gln Phe Glu Lys Lys Lys Asn Asp Thr Leu Asp Pro Glu Pro Phe  
 1265 1270 1275 1280  
 Val Asp Cys Lys Glu Cys Gly Arg Lys Met His Gln Ile Cys Val Leu  
 1285 1290 1295  
 His Tyr Asp Ile Ile Trp Pro Ser Gly Phe Val Cys Asp Asn Cys Leu  
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 Lys Lys Thr Gly Arg Pro Arg Lys Glu Asn Lys Phe Ser Ala Lys Arg  
 1315 1320 1325  
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 1330 1335 1340  
 Phe Leu Arg Arg Gln Asn His Pro Glu Ala Gly Glu Val Phe Val Arg  
 1345 1350 1355 1360  
 Val Val Ala Ser Ser Asp Lys Thr Val Glu Val Lys Pro Gly Met Lys  
 1365 1370 1375

203/299

Ser Arg Phe Val Asp Ser Gly Glu Met Ser Glu Ser Phe Pro Tyr Arg  
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 Thr Lys Ala Leu Phe Ala Phe Glu Glu Ile Asp Gly Val Asp Val Cys  
 1395 1400 1405  
 Phe Phe Gly Met His Val Gln Glu Tyr Gly Ser Asp Cys Pro Pro Pro  
 1410 1415 1420  
 Asn Thr Arg Arg Val Tyr Ile Ser Tyr Leu Asp Ser Ile His Phe Phe  
 1425 1430 1435 1440  
 Arg Pro Arg Cys Leu Arg Thr Ala Val Tyr His Glu Ile Leu Ile Gly  
 1445 1450 1455  
 Tyr Leu Glu Tyr Val Lys Lys Leu Gly Tyr Val Thr Gly His Ile Trp  
 1460 1465 1470  
 Ala Cys Pro Pro Ser Glu Gly Asp Asp Tyr Ile Phe His Cys His Pro  
 1475 1480 1485  
 Pro Asp Gln Lys Ile Pro Lys Pro Lys Arg Leu Gln Glu Trp Tyr Lys  
 1490 1495 1500  
 Lys Met Leu Asp Lys Ala Phe Ala Glu Arg Ile Ile His Asp Tyr Lys  
 1505 1510 1515 1520  
 Asp Ile Phe Lys Gln Ala Thr Glu Asp Arg Leu Thr Ser Ala Lys Glu  
 1525 1530 1535  
 Leu Pro Tyr Phe Glu Gly Asp Phe Trp Pro Asn Val Leu Glu Glu Ser  
 1540 1545 1550  
 Ile Lys Glu Leu Glu Gln Glu Glu Glu Glu Arg Lys Lys Glu Glu Ser  
 1555 1560 1565  
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 1570 1575 1580  
 Ala Lys Lys Lys Asn Asn Lys Lys Thr Asn Lys Asn Lys Ser Ser Ile  
 1585 1590 1595 1600  
 Ser Arg Ala Asn Lys Lys Lys Pro Ser Met Pro Asn Val Ser Asn Asp  
 1605 1610 1615  
 Leu Ser Gln Lys Leu Tyr Ala Thr Met Glu Lys His Lys Glu Val Phe  
 1620 1625 1630  
 Phe Val Ile His Leu His Ala Gly Pro Val Ile Asn Thr Leu Pro Pro  
 1635 1640 1645  
 Ile Val Asp Pro Asp Pro Leu Leu Ser Cys Asp Leu Met Asp Gly Arg  
 1650 1655 1660  
 Asp Ala Phe Leu Thr Leu Ala Arg Asp Lys His Trp Glu Phe Ser Ser  
 1665 1670 1675 1680  
 Leu Arg Arg Ser Lys Trp Ser Thr Leu Cys Met Leu Val Glu Leu His

204/299

1685	1690	1695
Thr Gln Gly Gln Asp Arg Phe Val Tyr Thr Cys Asn Glu Cys Lys His 1700	1705	1710
His Val Glu Thr Arg Trp His Cys Thr Val Cys Glu Asp Tyr Asp Leu 1715	1720	1725
Cys Ile Asn Cys Tyr Asn Thr Lys Ser His Ala His Lys Met Val Lys 1730	1735	1740
Trp Gly Leu Gly Leu Asp Asp Glu Gly Ser Ser Gln Gly Glu Pro Gln 1745	1750	1755 1760
Ser Lys Ser Pro Gln Glu Ser Arg Arg Leu Ser Ile Gln Arg Cys Ile 1765	1770	1775
Gln Ser Leu Val His Ala Cys Gln Cys Arg Asn Ala Asn Cys Ser Leu 1780	1785	1790
Pro Ser Cys Gln Lys Met Lys Arg Val Val Gln His Thr Lys Gly Cys 1795	1800	1805
Lys Arg Lys Thr Asn Gly Gly Cys Pro Val Cys Lys Gln Leu Ile Ala 1810	1815	1820
Leu Cys Cys Tyr His Ala Lys His Cys Gln Glu Asn Lys Cys Pro Val 1825	1830	1835 1840
Pro Phe Cys Leu Asn Ile Lys His Lys Leu Arg Gln Gln Gln Ile Gln 1845	1850	1855
His Arg Leu Gln Gln Ala Gln Leu Met Arg Arg Arg Met Ala Thr Met 1860	1865	1870
Asn Thr Arg Asn Val Pro Gln Gln Ser Leu Pro Ser Pro Thr Ser Ala 1875	1880	1885
Pro Pro Gly Thr Pro Thr Gln Gln Pro Ser Thr Pro Gln Thr Pro Gln 1890	1895	1900
Pro Pro Ala Gln Pro Gln Pro Ser Pro Val Ser Met Ser Pro Ala Gly 1905	1910	1915 1920
Phe Pro Ser Val Ala Arg Thr Gln Pro Pro Thr Thr Val Ser Thr Gly 1925	1930	1935
Lys Pro Thr Ser Gln Val Pro Ala Pro Pro Pro Pro Ala Gln Pro Pro 1940	1945	1950
Pro Ala Ala Val Glu Ala Ala Arg Gln Ile Glu Arg Glu Ala Gln Gln 1955	1960	1965
Gln Gln His Leu Tyr Arg Val Asn Ile Asn Asn Ser Met Pro Pro Gly 1970	1975	1980
Arg Thr Gly Met Gly Thr Pro Gly Ser Gln Met Ala Pro Val Ser Leu 1985	1990	1995 2000

205/299

Asn	Val	Pro	Arg	Pro	Asn	Gln	Val	Ser	Gly	Pro	Val	Met	Pro	Ser	Met	
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Pro	Pro	Gly	Gln	Trp	Gln	Gln	Ala	Pro	Leu	Pro	Gln	Gln	Gln	Pro	Met	
				2020					2025				2030			
Pro	Gly	Leu	Pro	Arg	Pro	Val	Ile	Ser	Met	Gln	Ala	Gln	Ala	Ala	Val	
				2035					2040				2045			
Ala	Gly	Pro	Arg	Met	Pro	Ser	Val	Gln	Pro	Pro	Arg	Ser	Ile	Ser	Pro	
				2050					2055				2060			
Ser	Ala	Leu	Gln	Asp	Leu	Leu	Arg	Thr	Leu	Lys	Ser	Pro	Ser	Ser	Pro	
2065				2070				2075				2080				
Gln	Gln	Gln	Gln	Gln	Val	Leu	Asn	Ile	Leu	Lys	Ser	Asn	Pro	Gln	Leu	
				2085					2090				2095			
Met	Ala	Ala	Phe	Ile	Lys	Gln	Arg	Thr	Ala	Lys	Tyr	Val	Ala	Asn	Gln	
				2100					2105				2110			
Pro	Gly	Met	Gln	Pro	Gln	Pro	Gly	Leu	Gln	Ser	Gln	Pro	Gly	Met	Gln	
				2115					2120				2125			
Pro	Gln	Pro	Gly	Met	His	Gln	Gln	Pro	Ser	Leu	Gln	Asn	Leu	Asn	Ala	
				2130					2135				2140			
Met	Gln	Ala	Gly	Val	Pro	Arg	Pro	Gly	Val	Pro	Pro	Gln	Gln	Gln	Ala	
2145				2150				2155				2160				
Met	Gly	Gly	Leu	Asn	Pro	Gln	Gly	Gln	Ala	Leu	Asn	Ile	Met	Asn	Pro	
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Gly	His	Asn	Pro	Asn	Met	Ala	Ser	Met	Asn	Pro	Gln	Tyr	Arg	Glu	Met	
				2180					2185				2190			
Leu	Arg	Arg	Gln	Leu	Leu	Gln	Gln	Gln	Gln	Gln	Gln	Gln	Gln	Gln	Gln	
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Gln	Gln	Gln	Gln	Gln	Gln	Gln	Gln	Gly	Ser	Ala	Gly	Met	Ala	Gly	Gly	
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Met	Ala	Gly	His	Gly	Gln	Phe	Gln	Gln	Pro	Gln	Gly	Pro	Gly	Gly	Tyr	
2225				2230				2235				2240				
Pro	Pro	Ala	Met	Gln	Gln	Gln	Arg	Met	Gln	Gln	His	Leu	Pro	Leu		
				2245					2250				2255			
Gln	Gly	Ser	Ser	Met	Gly	Gln	Met	Ala	Ala	Gln	Met	Gly	Gln	Leu	Gly	
				2260					2265				2270			
Gln	Met	Gly	Gln	Pro	Gly	Leu	Gly	Ala	Asp	Ser	Thr	Pro	Asn	Ile	Gln	
				2275					2280				2285			
Gln	Ala	Leu	Gln	Gln	Arg	Ile	Leu	Gln	Gln	Gln	Gln	Met	Lys	Gln	Gln	
				2290					2295				2300			

206/299

Ile Gly Ser Pro Gly Gln Pro Asn Pro Met Ser Pro Gln Gln His Met  
 2305 2310 2315 2320

Leu Ser Gly Gln Pro Gln Ala Ser His Leu Pro Gly Gln Gln Ile Ala  
 2325 2330 2335

Thr Ser Leu Ser Asn Gln Val Arg Ser Pro Ala Pro Val Gln Ser Pro  
 2340 2345 2350

Arg Pro Gln Ser Gln Pro Pro His Ser Ser Pro Ser Pro Arg Ile Gln  
 2355 2360 2365

Pro Gln Pro Ser Pro His His Val Ser Pro Gln Thr Gly Ser Pro His  
 2370 2375 2380

Pro Gly Leu Ala Val Thr Met Ala Ser Ser Ile Asp Gln Gly His Leu  
 2385 2390 2395 2400

Gly Asn Pro Glu Gln Ser Ala Met Leu Pro Gln Leu Asn Thr Pro Ser  
 2405 2410 2415

Arg Ser Ala Leu Ser Ser Glu Leu Ser Leu Val Gly Asp Thr Thr Gly  
 2420 2425 2430

Asp Thr Leu Glu Lys Phe Val Glu Gly Leu  
 2435 2440

&lt;210&gt; 253

&lt;211&gt; 8147

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 253

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207/299

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208/299

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&lt;210&gt; 254

&lt;211&gt; 183

209/299

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 254

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Leu His Val Pro Val Pro Arg Ala Leu Arg Met Glu Glu Asp Ser Ile
      35             40             45

Arg Leu Pro Ala His Leu Arg Leu Gln Pro Ile Tyr Trp Ser Arg Asp
      50             55             60

Asp Val Ala Gln Trp Leu Lys Trp Ala Glu Asn Glu Phe Ser Leu Arg
      65             70             75             80

Pro Ile Asp Ser Asn Thr Phe Glu Met Asn Gly Lys Ala Leu Leu Leu
      85             90             95

Leu Thr Lys Glu Asp Phe Arg Tyr Arg Ser Pro His Ser Gly Asp Val
      100            105            110

Leu Tyr Glu Leu Leu Gln His Ile Leu Lys Gln Arg Lys Pro Arg Ile
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Leu Phe Ser Pro Phe Phe His Pro Gly Asn Ser Ile His Thr Gln Pro
      130            135            140

Glu Val Ile Leu His Gln Asn His Glu Glu Glu Ala Leu Gln Arg Pro
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Val Ala Ser Asp Phe Glu Pro Gln Gly Leu Ser Glu Ala Ala Arg Trp
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Asn Ser Lys Glu Asn Leu Leu
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&lt;210&gt; 255

&lt;211&gt; 549

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 255

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cacacacagc cggagggtcat actgcatcag aaccatgaag aagaagccct tcagcggcca 480
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210/299

<210> 256  
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 <212> DNA  
 <213> Homo sapiens

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 agggctcttg tctgtcacc caggctggact gcagtggcac aatcacagct cactgcagcc 240  
 ttgagctcct ggtctcaagc aaccctccca cctcagcctc ccaagtagct ggggctgcag 300  
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 atttttacta gtttgcccg gccaagccag tgttgaacta ctggcctcaa gtgatcctcc 420  
 caccttggcc tccccaaagt gcatccctac aggcattgagc cactgcactc agcctgaact 480  
 ttcgaaattt attttaagg cccactttta aatgcttctt ttcagcagct aactttccag 540  
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 gaaaaacaaa aaaagaaaaa tttgtcgaat ccaggtgga atctgaatca agtgacttta 660  
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 <211> 604  
 <212> DNA  
 <213> Homo sapiens

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 tctgtgaact gaactcttct tgaacttttt gttgttggtg ttattggtgc ttttggagat 180  
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 atttttacta gtttgcccg gccaagccag tgttgaacta ctggcctcaa gtgatcctcc 420  
 caccttggcc tccccaaagt gcatccctac aggcattgagc cactgcactc agcctgaact 480  
 ttcgaaattt attttaagg cccactttta aatgcttctt ttcagcagct aactttccag 540  
 cggatgcttc atgtggtgcc agccatacag atacgctttt agaacttgag ctttggagaa 600  
 gctt 604

<210> 258  
 <211> 15  
 <212> PRT  
 <213> Homo sapiens

<400> 258  
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<210> 259  
 <211> 45  
 <212> DNA  
 <213> Homo sapiens

<400> 259  
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211/299

<210> 260  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 260  
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1 5 10 15

<210> 261  
<211> 45  
<212> DNA  
<213> Homo sapiens

<400> 261  
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<210> 262  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 262  
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1 5 10 15

<210> 263  
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<212> DNA  
<213> Homo sapiens

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<210> 264  
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<212> PRT  
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<210> 265  
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<212> DNA  
<213> Homo sapiens

<400> 265  
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212/299

&lt;210&gt; 266

&lt;211&gt; 829

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 266

Met Asn Ser Gly Val Ala Met Lys Tyr Gly Asn Asp Ser Ser Ala Glu  
 1 5 10 15

Leu Ser Glu Leu His Ser Ala Ala Leu Ala Ser Leu Lys Gly Asp Ile  
 20 25 30

Val Glu Leu Asn Lys Arg Leu Gln Gln Thr Glu Arg Glu Arg Asp Leu  
 35 40 45

Leu Glu Lys Lys Leu Ala Lys Ala Gln Cys Glu Gln Ser His Leu Met  
 50 55 60

Arg Glu His Glu Asp Val Gln Glu Arg Thr Thr Leu Arg Tyr Glu Glu  
 65 70 75 80

Arg Ile Thr Glu Leu His Ser Val Ile Ala Glu Leu Asn Lys Lys Ile  
 85 90 95

Asp Arg Leu Gln Gly Thr Thr Ile Arg Glu Glu Asp Glu Tyr Ser Glu  
 100 105 110

Leu Arg Ser Glu Leu Ser Gln Ser Gln His Glu Val Asn Glu Asp Ser  
 115 120 125

Arg Ser Met Asp Gln Asp Gln Thr Ser Val Ser Ile Pro Glu Asn Gln  
 130 135 140

Ser Thr Met Val Thr Ala Asp Met Asp Asn Cys Ser Asp Leu Asn Ser  
 145 150 155 160

Glu Leu Gln Arg Val Leu Thr Gly Leu Glu Asn Val Val Cys Gly Arg  
 165 170 175

Lys Lys Ser Ser Cys Ser Leu Ser Val Ala Glu Val Asp Arg His Ile  
 180 185 190

Glu Gln Leu Thr Thr Ala Ser Glu His Cys Asp Leu Ala Ile Lys Thr  
 195 200 205

Val Glu Glu Ile Glu Gly Val Leu Gly Arg Asp Leu Tyr Pro Asn Leu  
 210 215 220

Ala Glu Glu Arg Ser Arg Trp Glu Lys Glu Leu Ala Gly Leu Arg Glu  
 225 230 235 240

Glu Asn Glu Ser Leu Thr Ala Met Leu Cys Ser Lys Glu Glu Glu Leu  
 245 250 255

Asn Arg Thr Lys Ala Thr Met Asn Ala Ile Arg Glu Glu Arg Asp Arg  
 260 265 270

213/299

Leu Arg Arg Arg Val Arg Glu Leu Gln Thr Arg Leu Gln Ser Val Gln  
 275 280 285  
 Ala Thr Gly Pro Ser Ser Pro Gly Arg Leu Thr Ser Thr Asn Arg Pro  
 290 295 300  
 Ile Asn Pro Ser Thr Gly Glu Leu Ser Thr Ser Ser Ser Ser Asn Asp  
 305 310 315 320  
 Ile Pro Ile Ala Lys Ile Ala Glu Arg Val Lys Leu Ser Lys Thr Arg  
 325 330 335  
 Ser Glu Ser Ser Ser Ser Asp Arg Pro Val Leu Gly Ser Glu Ile Ser  
 340 345 350  
 Ser Ile Gly Val Ser Ser Ser Val Ala Glu His Leu Ala His Ser Leu  
 355 360 365  
 Gln Asp Cys Ser Asn Ile Gln Glu Ile Phe Gln Thr Leu Tyr Ser His  
 370 375 380  
 Gly Ser Ala Ile Ser Glu Ser Lys Ile Arg Glu Phe Glu Val Glu Thr  
 385 390 395 400  
 Glu Arg Leu Asn Ser Arg Ile Glu His Leu Lys Ser Gln Asn Asp Leu  
 405 410 415  
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 420 425 430  
 Met Leu Val Gly Lys Tyr Glu Ser Asn Ala Thr Ala Leu Arg Leu Ala  
 435 440 445  
 Leu Gln Tyr Ser Glu Gln Cys Ile Glu Ala Tyr Glu Leu Leu Leu Ala  
 450 455 460  
 Leu Ala Glu Ser Glu Gln Ser Leu Ile Leu Gly Gln Phe Arg Ala Ala  
 465 470 475 480  
 Gly Val Gly Ser Ser Pro Gly Asp Gln Ser Gly Asp Glu Asn Ile Thr  
 485 490 495  
 Gln Met Leu Lys Arg Ala His Asp Cys Arg Lys Thr Ala Glu Asn Ala  
 500 505 510  
 Ala Lys Ala Leu Leu Met Lys Leu Asp Gly Ser Cys Gly Gly Ala Phe  
 515 520 525  
 Ala Val Ala Gly Cys Ser Val Gln Pro Trp Glu Ser Leu Ser Ser Asn  
 530 535 540  
 Ser His Thr Ser Thr Thr Ser Ser Thr Ala Ser Ser Cys Asp Thr Glu  
 545 550 555 560  
 Phe Thr Lys Glu Asp Glu Gln Arg Leu Lys Asp Tyr Ile Gln Gln Leu  
 565 570 575  
 Lys Asn Asp Arg Ala Ala Val Lys Leu Thr Met Leu Glu Leu Glu Ser

214/299

580					585					590					
Ile	His	Ile	Asp	Pro	Leu	Ser	Tyr	Asp	Val	Lys	Pro	Arg	Gly	Asp	Ser
		595					600					605			
Gln	Arg	Leu	Asp	Leu	Glu	Asn	Ala	Val	Leu	Met	Gln	Glu	Leu	Met	Ala
	610					615					620				
Met	Lys	Glu	Glu	Met	Ala	Glu	Leu	Lys	Ala	Gln	Leu	Tyr	Leu	Leu	Glu
625					630					635					640
Lys	Glu	Lys	Lys	Ala	Leu	Glu	Leu	Lys	Leu	Ser	Thr	Arg	Glu	Ala	Gln
				645					650					655	
Glu	Gln	Ala	Tyr	Leu	Val	His	Ile	Glu	His	Leu	Lys	Ser	Glu	Val	Glu
			660					665					670		
Glu	Gln	Lys	Glu	Gln	Arg	Met	Arg	Ser	Leu	Ser	Ser	Thr	Ser	Ser	Gly
		675					680					685			
Ser	Lys	Asp	Lys	Pro	Gly	Lys	Glu	Cys	Ala	Asp	Ala	Ala	Ser	Pro	Ala
	690					695					700				
Leu	Ser	Leu	Ala	Glu	Leu	Arg	Thr	Thr	Cys	Ser	Glu	Asn	Glu	Leu	Ala
705					710					715					720
Ala	Glu	Phe	Thr	Asn	Ala	Ile	Arg	Arg	Glu	Lys	Lys	Leu	Lys	Ala	Arg
				725					730					735	
Val	Gln	Glu	Leu	Val	Ser	Ala	Leu	Glu	Arg	Leu	Thr	Lys	Ser	Ser	Glu
			740					745					750		
Ile	Arg	His	Gln	Gln	Ser	Ala	Glu	Phe	Val	Asn	Asp	Leu	Lys	Arg	Ala
		755					760					765			
Asn	Ser	Asn	Leu	Val	Ala	Ala	Tyr	Glu	Lys	Ala	Lys	Lys	Lys	His	Gln
	770					775					780				
Asn	Lys	Leu	Lys	Lys	Leu	Glu	Ser	Gln	Met	Met	Ala	Met	Val	Glu	Arg
785					790					795					800
His	Glu	Thr	Gln	Val	Arg	Met	Leu	Lys	Gln	Arg	Ile	Ala	Leu	Leu	Glu
				805					810					815	
Glu	Glu	Asn	Ser	Arg	Pro	His	Thr	Asn	Glu	Thr	Ser	Leu			
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&lt;210&gt; 267

&lt;211&gt; 4181

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 267

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tgtggcagaa gggaccaagc agtggatatt gagcctgtga agtccaactc ttaagctccg 180
agacctgggg gactgagagc ccagctctga aaagtgcac atgaattccg gagttgccat 240

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215/299

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216/299

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cgggtaggtc tatttttcaga gcatgataga aattccacag g 4181

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&lt;210&gt; 268

&lt;211&gt; 1172

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 268

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ggacagtttt tccgcagcct ctcggccacc accctcgaca gtggcggggc acggcgatct 180
gtgattgggt ctggccctca gctacttacc cactactatg atgatgcccg gaccatgtac 240
caggtgttcc gccgtgggct tagcatctca gggaaatgggc cctgtcttg tttcaggaag 300
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&lt;210&gt; 269

&lt;211&gt; 318

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 269

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Asn His Ile Met Val Ser Val Ser Pro Pro Glu Glu His Ala Met Pro
  1             5             10             15

Ile Gly Arg Ile Ala Asp Val Gln His Ile Lys Arg Arg Asp Ile Val
      20             25             30

Leu Lys Arg Glu Leu Gly Glu Gly Ala Phe Gly Lys Val Phe Leu Ala
      35             40             45

Glu Cys Tyr Asn Leu Ser Pro Thr Lys Asp Lys Met Leu Val Ala Val
      50             55             60

Lys Ala Leu Lys Asp Pro Thr Leu Ala Ala Arg Lys Asp Phe Gln Arg
      65             70             75             80

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217/299

Glu Ala Glu Leu Leu Thr Asn Leu Gln His Glu His Ile Val Lys Phe  
                                     85                                    90                                    95  
 Tyr Gly Val Cys Gly Asp Gly Asp Pro Leu Ile Met Val Phe Glu Tyr  
                                     100                                    105                                    110  
 Met Lys His Gly Asp Leu Asn Lys Phe Leu Arg Ala His Gly Pro Asp  
                                     115                                    120                                    125  
 Ala Met Ile Leu Val Asp Gly Gln Pro Arg Gln Ala Lys Gly Glu Leu  
                                     130                                    135                                    140  
 Gly Leu Ser Gln Met Leu His Ile Ala Ser Gln Ile Ala Ser Gly Met  
 145                                    150                                    155                                    160  
 Val Tyr Leu Ala Ser Gln His Phe Val His Arg Asp Leu Ala Thr Arg  
                                     165                                    170                                    175  
 Asn Cys Leu Val Gly Ala Asn Leu Leu Val Lys Ile Gly Asp Phe Gly  
                                     180                                    185                                    190  
 Met Ser Arg Asp Val Tyr Ser Thr Asp Tyr Tyr Arg Val Gly Gly His  
                                     195                                    200                                    205  
 Thr Met Leu Pro Ile Arg Trp Met Pro Pro Glu Ser Ile Met Tyr Arg  
                                     210                                    215                                    220  
 Lys Phe Thr Thr Glu Ser Asp Val Trp Ser Phe Gly Val Ile Leu Trp  
 225                                    230                                    235                                    240  
 Glu Ile Phe Thr Tyr Gly Lys Gln Pro Trp Phe Gln Leu Ser Asn Thr  
                                     245                                    250                                    255  
 Glu Val Ile Glu Cys Ile Thr Gln Gly Arg Val Leu Glu Arg Pro Arg  
                                     260                                    265                                    270  
 Val Cys Pro Lys Glu Val Tyr Asp Val Met Leu Gly Cys Trp Gln Arg  
                                     275                                    280                                    285  
 Glu Pro Gln Gln Arg Leu Asn Ile Lys Glu Ile Tyr Lys Ile Leu His  
                                     290                                    295                                    300  
 Ala Leu Gly Lys Ala Thr Pro Ile Tyr Leu Asp Ile Leu Gly  
 305                                    310                                    315

&lt;210&gt; 270

&lt;211&gt; 980

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 270

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 gcagatgtgc agcacattaa gaggagagac atcgtgtctga agcgagaact ggggtgagggg 120  
 gccttttgaa aggtcttcct ggccgagtgc tacaacctca gcccgaccaa ggacaagatg 180  
 cttgtggctg tgaaggccct gaaggatccc accctggctg cccggaagga ttccagagg 240  
 gaggccgagc tgctcaccaa cctgcagcat gagcacattg tcaagttcta tggagtgtgc 300



218/299

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ggcgatgggg acccctcat catggtcttt gaatacatga agcatggaga cctgaataag 360
ttcctcaggg cccatgggcc agatgcaatg atccttgtgg atggacagcc acgccaggcc 420
aagggtgagc tggggctctc ccaaagtctc cacattgcca gtcagatcgc ctcggtatg 480
gtgtacctgg cctcccagca ctttgtgcac cgagacctgg ccaccaggaa ctgcctggtt 540
ggagcgaatc tgctagttaa gattggggac ttgggcatgt ccagagatgt ctacagcacg 600
gattattaca ggggtgggagg acacaccatg ctccccattc gctggatgcc tcctgaaagc 660
atcatgtacc ggaagtccac tacagagagt gatgtatgga gcttcggggg gatcctctgg 720
gagatcttca cctatggaaa gcagccatgg ttccaactct caaacacgga ggtcatttag 780
tgcattaccc aaggtcgtgt tttggagcgg ccccgagtct gcccacaaaga ggtgtacgat 840
gtcatgctgg ggtgctggca gagggaaacca cagcagcggg tgaacatcaa ggagatctac 900
aaaatcctcc atgctttggg gaaggccacc ccaatctacc tggacattct tggctagtgg 960
tggctggtgg tcatgaattc

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&lt;210&gt; 271

&lt;211&gt; 408

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 271

```

Glu Asn Asn His Gln Glu Ser Tyr Pro Leu Ser Val Ser Pro Met Glu
 1              5              10              15

Asn Asn His Cys Pro Ala Ser Ser Glu Ser His Pro Lys Pro Ser Ser
      20              25              30

Pro Arg Gln Glu Ser Thr Arg Val Ile Gln Leu Met Pro Ser Pro Ile
      35              40              45

Met His Pro Leu Ile Leu Asn Pro Arg His Ser Val Asp Phe Lys Gln
      50              55              60

Ser Arg Leu Ser Glu Asp Gly Leu His Arg Glu Gly Lys Pro Ile Asn
      65              70              75              80

Leu Ser His Arg Glu Asp Leu Ala Tyr Met Asn His Ile Met Val Ser
      85              90              95

Val Ser Pro Pro Glu Glu His Ala Met Pro Ile Gly Arg Ile Ala Asp
      100              105              110

Val Gln His Ile Lys Arg Arg Asp Ile Val Leu Lys Arg Glu Leu Gly
      115              120              125

Glu Gly Ala Phe Gly Lys Val Phe Leu Ala Glu Cys Tyr Asn Leu Ser
      130              135              140

Pro Thr Lys Asp Lys Met Leu Val Ala Val Lys Ala Leu Lys Asp Pro
      145              150              155              160

Thr Leu Ala Ala Arg Lys Asp Phe Gln Arg Glu Ala Glu Leu Leu Thr
      165              170              175

Asn Leu Gln His Glu His Ile Val Lys Phe Tyr Gly Val Cys Gly Asp
      180              185              190

Gly Asp Pro Leu Ile Met Val Phe Glu Tyr Met Lys His Gly Asp Leu
      195              200              205

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219/299

Asn Lys Phe Leu Arg Ala His Gly Pro Asp Ala Met Ile Leu Val Asp  
 210 215 220  
 Gly Gln Pro Arg Gln Ala Lys Gly Glu Leu Gly Leu Ser Gln Met Leu  
 225 230 235 240  
 His Ile Ala Ser Gln Ile Ala Ser Gly Met Val Tyr Leu Ala Ser Gln  
 245 250 255  
 His Phe Val His Arg Asp Leu Ala Thr Arg Asn Cys Leu Val Gly Ala  
 260 265 270  
 Asn Leu Leu Val Lys Ile Gly Asp Phe Gly Met Ser Arg Asp Val Tyr  
 275 280 285  
 Ser Thr Asp Tyr Tyr Arg Val Gly Gly His Thr Met Leu Pro Ile Arg  
 290 295 300  
 Trp Met Pro Pro Glu Ser Ile Met Tyr Arg Lys Phe Thr Thr Glu Ser  
 305 310 315 320  
 Asp Val Trp Ser Phe Gly Val Ile Leu Trp Glu Ile Phe Thr Tyr Gly  
 325 330 335  
 Lys Gln Pro Trp Phe Gln Leu Ser Asn Thr Glu Val Ile Glu Cys Ile  
 340 345 350  
 Thr Gln Gly Arg Val Leu Glu Arg Pro Arg Val Cys Pro Lys Glu Val  
 355 360 365  
 Tyr Asp Val Met Leu Gly Cys Trp Gln Arg Glu Pro Gln Gln Arg Leu  
 370 375 380  
 Asn Ile Lys Glu Ile Tyr Lys Ile Leu His Ala Leu Gly Lys Ala Thr  
 385 390 395 400  
 Pro Ile Tyr Leu Asp Ile Leu Gly  
 405

&lt;210&gt; 272

&lt;211&gt; 1403

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 272

gagaacaacc accaggagtc ctaccctctg tcagtgtctc ccatggagaa taatcactgc 60  
 ccagcgtcct ccgagtccca cccgaagcca tccagccccc ggcaggagag cacacgcgtg 120  
 atccagctga tgcccagccc catcatgcac cctctgatcc tgaacccccg gcactccgtg 180  
 gatttcaaac agtccaggct ctccgaggac gggctgcata ggggaaggga gcccatcaac 240  
 ctctctcatc gggaagacct ggcttacatg aaccacatca tggctctctgt ctccccgcct 300  
 gaagagcacg ccatgcccat tgggagaata gcagatgtgc agcacattaa gaggagagac 360  
 atcgtgctga agcgagaact ggggtgaggga gcctttggaa aggtcttcct ggccgagtgc 420  
 tacaacctca gcccgaccaa ggacaagatg cttgtggctg tgaaggccct gaaggatccc 480  
 accctggctg cccggaagga tttccagagg gaggccgagc tgctcaccaa cctgcagcat 540  
 gagcacattg tcaagttcta tggagtgtgc ggcgatgggg accccctcat catggctctt 600  
 gaatacatga agcatggaga cctgaataag ttccctcaggg cccatgggcc agatgcaatg 660

220/299

```

atccttgtgg atggacagcc acgccaggcc aaggggtgagc tggggctctc ccaaagtctc 720
cacattgccg gtcagatcgc ctcggttatg gtgtacctgg cctcccagca ctttgtgcac 780
cgagacctgg ccaccaggaa ctgcctggtt ggagcgaatc tgctagttaa gattggggac 840
ttcggcatgt ccagagatgt ctacagcacg gattattaca ggggtgggagg acacaccatg 900
ctcccattc gctggatgcc tcctgaaagc atcatgtacc ggaagtccac tacagagagt 960
gatgtatgga gcttcggggg gatcctctgg gagatcttca cctatggaaa gcagccatgg 1020
ttccaactct caaacacgga ggtcattgag tgcattaccc aaggtcgtgt tttggagcgg 1080
ccccgagtct gcccacaaaga ggtgtacgat gtcattgctgg ggtgctggca gaggggaacca 1140
cagcagcggg tgaacatcaa ggagatctac aaaatcctcc atgctttggg gaaggccacc 1200
ccaatctacc tggacattct tggctagtgg tggctgggtg tcatgaattc atactctgtt 1260
gcctcctctc tcctgcctc acatctccct tccacctcac aactccttcc atccttgact 1320
gaagcgaaca tcttcatata aactcaagtg cctgctacac atacaacact gaaaaaagga 1380
aaaaaaaaga aaaaaaaaaa aaa 1403

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&lt;210&gt; 273

&lt;211&gt; 536

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 273

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Met Gly Ser Asn Lys Ser Lys Pro Lys Asp Ala Ser Gln Arg Arg Arg
 1              5              10              15

Ser Leu Glu Pro Ala Glu Asn Val His Gly Ala Gly Gly Gly Ala Phe
          20              25              30

Pro Ala Ser Gln Thr Pro Ser Lys Pro Ala Ser Ala Asp Gly His Arg
      35              40              45

Gly Pro Ser Ala Ala Phe Ala Pro Ala Ala Ala Glu Pro Lys Leu Phe
 50              55              60

Gly Gly Phe Asn Ser Ser Asp Thr Val Thr Ser Pro Gln Arg Ala Gly
 65              70              75              80

Pro Leu Ala Gly Gly Val Thr Thr Phe Val Ala Leu Tyr Asp Tyr Glu
          85              90              95

Ser Arg Thr Glu Thr Asp Leu Ser Phe Lys Lys Gly Glu Arg Leu Gln
      100              105              110

Ile Val Asn Asn Thr Glu Gly Asp Trp Trp Leu Ala His Ser Leu Ser
      115              120              125

Thr Gly Gln Thr Gly Tyr Ile Pro Ser Asn Tyr Val Ala Pro Ser Asp
      130              135              140

Ser Ile Gln Ala Glu Glu Trp Tyr Phe Gly Lys Ile Thr Arg Arg Glu
      145              150              155              160

Ser Glu Arg Leu Leu Leu Asn Ala Glu Asn Pro Arg Gly Thr Phe Leu
          165              170              175

Val Arg Glu Ser Glu Thr Thr Lys Gly Ala Tyr Cys Leu Ser Val Ser
      180              185              190

Asp Phe Asp Asn Ala Lys Gly Leu Asn Val Lys His Tyr Lys Ile Arg

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221/299

195					200					205					
Lys	Leu	Asp	Ser	Gly	Gly	Phe	Tyr	Ile	Thr	Ser	Arg	Thr	Gln	Phe	Asn
210					215					220					
Ser	Leu	Gln	Gln	Leu	Val	Ala	Tyr	Tyr	Ser	Lys	His	Ala	Asp	Gly	Leu
225					230					235					240
Cys	His	Arg	Leu	Thr	Thr	Val	Cys	Pro	Thr	Ser	Lys	Pro	Gln	Thr	Gln
				245					250					255	
Gly	Leu	Ala	Lys	Asp	Ala	Trp	Glu	Ile	Pro	Arg	Glu	Ser	Leu	Arg	Leu
			260					265					270		
Glu	Val	Lys	Leu	Gly	Gln	Gly	Cys	Phe	Gly	Glu	Val	Trp	Met	Gly	Thr
		275					280					285			
Trp	Asn	Gly	Thr	Thr	Arg	Val	Ala	Ile	Lys	Thr	Leu	Lys	Pro	Gly	Thr
	290					295					300				
Met	Ser	Pro	Glu	Ala	Phe	Leu	Gln	Glu	Ala	Gln	Val	Met	Lys	Lys	Leu
305					310					315					320
Arg	His	Glu	Lys	Leu	Val	Gln	Leu	Tyr	Ala	Val	Val	Ser	Glu	Glu	Pro
				325					330					335	
Ile	Tyr	Ile	Val	Thr	Glu	Tyr	Met	Ser	Lys	Gly	Ser	Leu	Leu	Asp	Phe
			340					345				350			
Leu	Lys	Gly	Glu	Thr	Gly	Lys	Tyr	Leu	Arg	Leu	Pro	Gln	Leu	Val	Asp
		355					360					365			
Met	Ala	Ala	Gln	Ile	Ala	Ser	Gly	Met	Ala	Tyr	Val	Glu	Arg	Met	Asn
	370					375					380				
Tyr	Val	His	Arg	Asp	Leu	Arg	Ala	Ala	Asn	Ile	Leu	Val	Gly	Glu	Asn
385					390					395					400
Leu	Val	Cys	Lys	Val	Ala	Asp	Phe	Gly	Leu	Ala	Arg	Leu	Ile	Glu	Asp
				405					410					415	
Asn	Glu	Tyr	Thr	Ala	Arg	Gln	Gly	Ala	Lys	Phe	Pro	Ile	Lys	Trp	Thr
			420					425					430		
Ala	Pro	Glu	Ala	Ala	Leu	Tyr	Gly	Arg	Phe	Thr	Ile	Lys	Ser	Asp	Val
		435					440					445			
Trp	Ser	Phe	Gly	Ile	Leu	Leu	Thr	Glu	Leu	Thr	Thr	Lys	Gly	Arg	Val
	450					455					460				
Pro	Tyr	Pro	Gly	Met	Val	Asn	Arg	Glu	Val	Leu	Asp	Gln	Val	Glu	Arg
465					470					475					480
Gly	Tyr	Arg	Met	Pro	Cys	Pro	Pro	Glu	Cys	Pro	Glu	Ser	Leu	His	Asp
				485					490					495	
Leu	Met	Cys	Gln	Cys	Trp	Arg	Lys	Glu	Pro	Glu	Glu	Arg	Pro	Thr	Phe
			500					505					510		

222/299

Glu Tyr Leu Gln Ala Phe Leu Glu Asp Tyr Phe Thr Ser Thr Glu Pro  
 515 520 525

Gln Tyr Gln Pro Gly Glu Asn Leu  
 530 535

<210> 274  
 <211> 1611  
 <212> DNA  
 <213> Homo sapiens

<400> 274  
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 ccagcctcgg ccgacggcca ccgcgggccc agcgcgccct tcgccccgcg ggccgcccag 180  
 cccaagctgt tcggaggcct caactcctcg gacaccgtca cctccccgca gagggcgggc 240  
 ccgctggccg gtggagtgac cacctttgtg gccctctatg actatgagtc taggacggag 300  
 acagacctgt ccttcaagaa aggcgagcgg ctccagattg tcaacaacac agaggagagac 360  
 tgggtggctgg cccactcgtc cagcacagga cagacaggct acatccccag caactacgtg 420  
 gcgcccctccg actccatcca ggctgaggag tggatatttg gcaagatcac cagacgggag 480  
 tcagagcggg tactgtctca tgcagagaac ccgagaggga ccttcctcgt gcgagaaaagt 540  
 gagaccacga aaggtgccta ctgcctctca gtgtctgact tcgacaacgc caagggcctc 600  
 aacgtgaagc actacaagat ccgcaagctg gacagcggcg gcttctacat cacctccgcg 660  
 acccagttca acagcctgca gcagctggtg gcctactact ccaaacacgc cgatggcctg 720  
 tgccaccgcc tcaccaccgt gtgccccacg tccaagccgc agactcaggg cctggccaag 780  
 gatgcctggg agatccctcg ggagtcgctg cggctggagg tcaagctggg ccagggctgc 840  
 tttggcgagg tgtggatggg gacctggaac ggtaccacca ggggtggccat caaaacctg 900  
 aagcctggca cgatgtctcc agaggccttc ctgcaggagg cccagggtcat gaagaagctg 960  
 aggcattgaga agctggtgca gttgtatgct gtggtttcag aggagcccat ttacatcgtc 1020  
 acggagtaca tgagcaaggg gagtttctcg gactttctca aggggggagac aggcaagtac 1080  
 ctgcggctgc ctgagctggt ggacatggct gctcagatcg cctcaggcat ggcgtacgtg 1140  
 gagcggatga actacgtcca ccgggacctt cgtgcagcca acatcctggt gggagagaac 1200  
 ctggtgtgca aagtggccga ctttgggctg gctcggctca ttgaagacaa tgagtacacg 1260  
 gcgcggaag gtgccaaatt ccccatcaag tggacggctc cagaagctgc cctctatggc 1320  
 cgcttcacca tcaagtccga cgtgtggctc ttccgggatcc tgctgactga gctcaccaca 1380  
 aagggaacgg tgccctaccc tgggatgggt aaccgcgagg tgctggacca ggtggagcgg 1440  
 ggctaccgga tgccctgccc gccggagtgt cccgagtccc tgcacgacct catgtgccag 1500  
 tgctggcgga aggagcctga ggagcggccc accttcaggt acctgcaggc cttcctggag 1560  
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<210> 275  
 <211> 226  
 <212> PRT  
 <213> Homo sapiens

<400> 275  
 Met Tyr His Ala Ser Lys Leu Ser Ile Asp Glu Glu Val Tyr Phe Glu  
 1 5 10 15  
 Asn Leu Met Gln Leu Val Glu His Tyr Thr Ser Asp Ala Asp Gly Leu  
 20 25 30  
 Cys Thr Arg Leu Ile Lys Pro Lys Val Met Glu Gly Thr Val Ala Ala  
 35 40 45

223/299

Gln Asp Glu Phe Tyr Arg Ser Gly Trp Ala Leu Asn Met Lys Glu Leu  
     50                                    55                                    60  
 Lys Leu Leu Gln Thr Ile Gly Lys Gly Glu Phe Gly Asp Val Met Leu  
     65                                    70                                    75                                    80  
 Gly Asp Tyr Arg Gly Asn Lys Val Ala Val Lys Cys Ile Lys Asn Asp  
                                     85                                    90                                    95  
 Ala Thr Ala Gln Ala Phe Leu Ala Glu Ala Ser Val Met Thr Gln Leu  
                     100                                    105                                    110  
 Arg His Ser Asn Leu Val Gln Leu Leu Gly Val Ile Val Glu Glu Lys  
                     115                                    120                                    125  
 Gly Gly Leu Tyr Ile Val Thr Glu Tyr Met Ala Lys Gly Ser Leu Val  
     130                                    135                                    140  
 Asp Tyr Leu Arg Ser Arg Gly Arg Ser Val Leu Gly Gly Asp Cys Leu  
     145                                    150                                    155                                    160  
 Leu Lys Phe Ser Leu Asp Val Cys Glu Ala Met Glu Tyr Leu Glu Gly  
                     165                                    170                                    175  
 Asn Asn Phe Val His Arg Asp Leu Ala Ala Arg Asn Val Leu Val Ser  
                     180                                    185                                    190  
 Glu Asp Asn Val Ala Lys Val Ser Asp Phe Gly Leu Thr Lys Glu Ala  
                     195                                    200                                    205  
 Ser Thr Pro Arg Thr Arg Ala Ser Cys Gln Ser Ser Gly Gln Pro Leu  
     210                                    215                                    220  
 Arg Pro  
 225

&lt;210&gt; 276

&lt;211&gt; 2442

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 276

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 cggaagcgga actctgccgg ggccgcgcgg gctacattgt gctgcggtcg actctagagg 120  
 ctcccccttc tccccccgac tccctccctc ccccttcccc cgcctttctt ccctccgcga 180  
 cccggggcgt gcgtccgtcc cctgcctct gcttggcggt ccctcctccc ctctccttgc 240  
 acccatacct ctttgtaccg caccacctgg gtatccctgc gccctcccc tccccctga 300  
 ccgcatggac cgtcccgag gccgctgatg ccgcccgcgg gacggtggcc cggaccgcag 360  
 tgccccaaga gagctctaag ggtaccaagt gacaggttgg cttaactgag actcggggac 420  
 ccaagagctc ctgagaagat gtcagcaata caggccgcct ggccatccgg tacagaatgt 480  
 attgccaagt acaacttcca cggcactgcc gagcaggacc tgcccttctg caaaggagac 540  
 gtgctcacca ttgtggccgt caccaaggac cccaactggg acaaagccaa aaacaagggtg 600  
 ggccgtgagg gcatcatccc agccaactac gtccagaagc gggagggcgt gaaggcgggt 660  
 accaaactca gcctcatgcc gtgagttcca cggcaagatc acacgggagc aggctgagcg 720  
 gcttctgtac ccgcccggaga caggcctgtt cctggtgcgg gagagcacca actaccccg 780  
 agactacacg ctgtgcgtga gctgcgacgg caaggtggag cactaccgca tcatgtacca 840  
 tgccagcaag ctcagcatcg acgaggaggt gtactttgag aacctcatgc agctggtgga 900

224/299

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gcactacacc tcagacgcag atggactctg tacgcgcctc attaaaccaa aggtcatgga 960
gggcacagtg gcggcccagg atgagttcta ccgcagcggc tgggccctga acatgaagga 1020
gctgaagctg ctgcagacca tcgggaaggg ggagttcgga gacgtgatgc tgggcgatta 1080
ccgaggggaac aaagtcgccc tcaagtgcac taagaacgac gccactgccc aggccttcct 1140
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gatcgtggag gagaagggcg ggctctacat cgtcactgag tacatggcca aggggagcct 1260
tgtggactac ctgcggtcta ggggtcggtc agtgctgggc ggagactgtc tcctcaagtt 1320
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tctcaccaag gaggcgtcca caccaggac acgggcaagc tgccagtcaa gtggacagcc 1500
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gctcactggg cccgagcctg aactgagccc cagcgggctg gcgggccttt ttctgcgtc 1920
ccagcctgca cccctccggc cccgtctctc ttggaccacac ctgtggggcc tggggagccc 1980
actgaggggc cagggaggaa ggaggccacg gagcgggagg cagcgcccca ccacgtcggg 2040
cttccctggc ctcccgccac tcgccttctt agagttttat tcctttcctt ttttgagatt 2100
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gcgcccagag cagacgtctg tcaggggctt ggatttcgtg tgccgctgcc acccgccac 2400
ccgccttggt agatggaatt gtaataaacc acgcatgag ga 2442

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&lt;210&gt; 277

&lt;211&gt; 1114

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 277

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Met Ala Lys Ala Thr Ser Gly Ala Ala Gly Leu Arg Leu Leu Leu Leu
  1                      5                      10                      15

Leu Leu Leu Pro Leu Leu Gly Lys Val Ala Leu Gly Leu Tyr Phe Ser
      20                      25                      30

Arg Asp Ala Tyr Trp Glu Lys Leu Tyr Val Asp Gln Ala Ala Gly Thr
      35                      40                      45

Pro Leu Leu Tyr Val His Ala Leu Arg Asp Ala Pro Glu Glu Val Pro
      50                      55                      60

Ser Phe Arg Leu Gly Gln His Leu Tyr Gly Thr Tyr Arg Thr Arg Leu
      65                      70                      75                      80

His Glu Asn Asn Trp Ile Cys Ile Gln Glu Asp Thr Gly Leu Leu Tyr
      85                      90                      95

Leu Asn Arg Ser Leu Asp His Ser Ser Trp Glu Lys Leu Ser Val Arg
      100                      105                      110

Asn Arg Gly Phe Pro Leu Leu Thr Val Tyr Leu Lys Val Phe Leu Ser
      115                      120                      125

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225/299

Pro Thr Ser Leu Arg Glu Gly Glu Cys Gln Trp Pro Gly Cys Ala Arg  
 130 135 140  
 Val Tyr Phe Ser Phe Phe Asn Thr Ser Phe Pro Ala Cys Ser Ser Leu  
 145 150 155 160  
 Lys Pro Arg Glu Leu Cys Phe Pro Glu Thr Arg Pro Ser Phe Arg Ile  
 165 170 175  
 Arg Glu Asn Arg Pro Pro Gly Thr Phe His Gln Phe Arg Leu Leu Pro  
 180 185 190  
 Val Gln Phe Leu Cys Pro Asn Ile Ser Val Ala Tyr Arg Leu Leu Glu  
 195 200 205  
 Gly Glu Gly Leu Pro Phe Arg Cys Ala Pro Asp Ser Leu Glu Val Ser  
 210 215 220  
 Thr Arg Trp Ala Leu Asp Arg Glu Gln Arg Glu Lys Tyr Glu Leu Val  
 225 230 235 240  
 Ala Val Cys Thr Val His Ala Gly Ala Arg Glu Glu Val Val Met Val  
 245 250 255  
 Pro Phe Pro Val Thr Val Tyr Asp Glu Asp Asp Ser Ala Pro Thr Phe  
 260 265 270  
 Pro Ala Gly Val Asp Thr Ala Ser Ala Val Val Glu Phe Lys Arg Lys  
 275 280 285  
 Glu Asp Thr Val Val Ala Thr Leu Arg Val Phe Asp Ala Asp Val Val  
 290 295 300  
 Pro Ala Ser Gly Glu Leu Val Arg Arg Tyr Thr Ser Thr Leu Leu Pro  
 305 310 315 320  
 Gly Asp Thr Trp Ala Gln Gln Thr Phe Arg Val Glu His Trp Pro Asn  
 325 330 335  
 Glu Thr Ser Val Gln Ala Asn Gly Ser Phe Val Arg Ala Thr Val His  
 340 345 350  
 Asp Tyr Arg Leu Val Leu Asn Arg Asn Leu Ser Ile Ser Glu Asn Arg  
 355 360 365  
 Thr Met Gln Leu Ala Val Leu Val Asn Asp Ser Asp Phe Gln Gly Pro  
 370 375 380  
 Gly Ala Gly Val Leu Leu Leu His Phe Asn Val Ser Val Leu Pro Val  
 385 390 395 400  
 Ser Leu His Leu Pro Ser Thr Tyr Ser Leu Ser Val Ser Arg Arg Ala  
 405 410 415  
 Arg Arg Phe Ala Gln Ile Gly Lys Val Cys Val Glu Asn Cys Gln Ala  
 420 425 430  
 Phe Ser Gly Ile Asn Val Gln Tyr Lys Leu His Ser Ser Gly Ala Asn



226/299

435					440					445					
Cys	Ser	Thr	Leu	Gly	Val	Val	Thr	Ser	Ala	Glu	Asp	Thr	Ser	Gly	Ile
450						455					460				
Leu	Phe	Val	Asn	Asp	Thr	Lys	Ala	Leu	Arg	Arg	Pro	Lys	Cys	Ala	Glu
465					470					475					480
Leu	His	Tyr	Met	Val	Val	Ala	Thr	Asp	Gln	Gln	Thr	Ser	Arg	Gln	Ala
				485					490					495	
Gln	Ala	Gln	Leu	Leu	Val	Thr	Val	Glu	Gly	Ser	Tyr	Val	Ala	Glu	Glu
			500					505					510		
Ala	Gly	Cys	Pro	Leu	Ser	Cys	Ala	Val	Ser	Lys	Arg	Arg	Leu	Glu	Cys
		515					520					525			
Glu	Glu	Cys	Gly	Gly	Leu	Gly	Ser	Pro	Thr	Gly	Arg	Cys	Glu	Trp	Arg
530					535					540					
Gln	Gly	Asp	Gly	Lys	Gly	Ile	Thr	Arg	Asn	Phe	Ser	Thr	Cys	Ser	Pro
545				550					555					560	
Ser	Thr	Lys	Thr	Cys	Pro	Asp	Gly	His	Cys	Asp	Val	Val	Glu	Thr	Gln
				565					570					575	
Asp	Ile	Asn	Ile	Cys	Pro	Gln	Asp	Cys	Leu	Arg	Gly	Ser	Ile	Val	Gly
			580					585					590		
Gly	His	Glu	Pro	Gly	Glu	Pro	Arg	Gly	Ile	Lys	Ala	Gly	Tyr	Gly	Thr
		595					600					605			
Cys	Asn	Cys	Phe	Pro	Glu	Glu	Glu	Lys	Cys	Phe	Cys	Glu	Pro	Glu	Asp
610					615					620					
Ile	Gln	Asp	Pro	Leu	Cys	Asp	Glu	Leu	Cys	Arg	Thr	Val	Ile	Ala	Ala
625				630					635					640	
Ala	Val	Leu	Phe	Ser	Phe	Ile	Val	Ser	Val	Leu	Leu	Ser	Ala	Phe	Cys
				645					650					655	
Ile	His	Cys	Tyr	His	Lys	Phe	Ala	His	Lys	Pro	Pro	Ile	Ser	Ser	Ala
			660					665					670		
Glu	Met	Thr	Phe	Arg	Arg	Pro	Ala	Gln	Ala	Phe	Pro	Val	Ser	Tyr	Ser
		675					680					685			
Ser	Ser	Gly	Ala	Arg	Arg	Pro	Ser	Leu	Asp	Ser	Met	Glu	Asn	Gln	Val
690					695					700					
Ser	Val	Asp	Ala	Phe	Lys	Ile	Leu	Glu	Asp	Pro	Lys	Trp	Glu	Phe	Pro
705				710					715					720	
Arg	Lys	Asn	Leu	Val	Leu	Gly	Lys	Thr	Leu	Gly	Glu	Gly	Glu	Phe	Gly
			725					730						735	
Lys	Val	Val	Lys	Ala	Thr	Ala	Phe	His	Leu	Lys	Gly	Arg	Ala	Gly	Tyr
			740					745					750		

Thr	Thr	Val	Ala	Val	Lys	Met	Leu	Lys	Glu	Asn	Ala	Ser	Pro	Ser	Glu
		755					760					765			
Leu	Arg	Asp	Leu	Leu	Ser	Glu	Phe	Asn	Val	Leu	Lys	Gln	Val	Asn	His
	770					775					780				
Pro	His	Val	Ile	Lys	Leu	Tyr	Gly	Ala	Cys	Ser	Gln	Asp	Gly	Pro	Leu
785					790					795					800
Leu	Leu	Ile	Val	Glu	Tyr	Ala	Lys	Tyr	Gly	Ser	Leu	Arg	Gly	Phe	Leu
				805					810					815	
Arg	Glu	Ser	Arg	Lys	Val	Gly	Pro	Gly	Tyr	Leu	Gly	Ser	Gly	Gly	Ser
			820					825					830		
Arg	Asn	Ser	Ser	Ser	Leu	Asp	His	Pro	Asp	Glu	Arg	Ala	Leu	Thr	Met
		835					840					845			
Gly	Asp	Leu	Ile	Ser	Phe	Ala	Trp	Gln	Ile	Ser	Gln	Gly	Met	Gln	Tyr
	850					855					860				
Leu	Ala	Glu	Met	Lys	Leu	Val	His	Arg	Asp	Leu	Ala	Ala	Arg	Asn	Ile
865					870					875					880
Leu	Val	Ala	Glu	Gly	Arg	Lys	Met	Lys	Ile	Ser	Asp	Phe	Gly	Leu	Ser
				885					890					895	
Arg	Asp	Val	Tyr	Glu	Glu	Asp	Ser	Tyr	Val	Lys	Arg	Ser	Gln	Gly	Arg
			900					905					910		
Ile	Pro	Val	Lys	Trp	Met	Ala	Ile	Glu	Ser	Leu	Phe	Asp	His	Ile	Tyr
		915					920					925			
Thr	Thr	Gln	Ser	Asp	Val	Trp	Ser	Phe	Gly	Val	Leu	Leu	Trp	Glu	Ile
	930					935					940				
Val	Thr	Leu	Gly	Gly	Asn	Pro	Tyr	Pro	Gly	Ile	Pro	Pro	Glu	Arg	Leu
945					950					955					960
Phe	Asn	Leu	Leu	Lys	Thr	Gly	His	Arg	Met	Glu	Arg	Pro	Asp	Asn	Cys
				965					970					975	
Ser	Glu	Glu	Met	Tyr	Arg	Leu	Met	Leu	Gln	Cys	Trp	Lys	Gln	Glu	Pro
			980					985					990		
Asp	Lys	Arg	Pro	Val	Phe	Ala	Asp	Ile	Ser	Lys	Asp	Leu	Glu	Lys	Met
		995				1000					1005				
Met	Val	Lys	Arg	Arg	Asp	Tyr	Leu	Asp	Leu	Ala	Ala	Ser	Thr	Pro	Ser
	1010					1015				1020					
Asp	Ser	Leu	Ile	Tyr	Asp	Asp	Gly	Leu	Ser	Glu	Glu	Glu	Thr	Pro	Leu
1025					1030					1035					1040
Val	Asp	Cys	Asn	Asn	Ala	Pro	Leu	Pro	Arg	Ala	Leu	Pro	Ser	Thr	Trp
			1045						1050					1055	

228/299

Ile Glu Asn Lys Leu Tyr Gly Met Ser Asp Pro Asn Trp Pro Gly Glu  
 1060 1065 1070

Ser Pro Val Pro Leu Thr Arg Ala Asp Gly Thr Asn Thr Gly Phe Pro  
 1075 1080 1085

Arg Tyr Pro Asn Asp Ser Val Tyr Ala Asn Trp Met Leu Ser Pro Ser  
 1090 1095 1100

Ala Ala Lys Leu Met Asp Thr Phe Asp Ser  
 1105 1110

&lt;210&gt; 278

&lt;211&gt; 393

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 278

Met Glu Glu Pro Gln Ser Asp Pro Ser Val Glu Pro Pro Leu Ser Gln  
 1 5 10 15

Glu Thr Phe Ser Asp Leu Trp Lys Leu Leu Pro Glu Asn Asn Val Leu  
 20 25 30

Ser Pro Leu Pro Ser Gln Ala Met Asp Asp Leu Met Leu Ser Pro Asp  
 35 40 45

Asp Ile Glu Gln Trp Phe Thr Glu Asp Pro Gly Pro Asp Glu Ala Pro  
 50 55 60

Arg Met Pro Glu Ala Ala Pro Pro Val Ala Pro Ala Pro Ala Thr Pro  
 65 70 75 80

Thr Pro Ala Ala Pro Ala Pro Ala Pro Ser Trp Pro Leu Ser Ser Ser  
 85 90 95

Val Pro Ser Gln Lys Thr Tyr Gln Gly Ser Tyr Gly Phe Arg Leu Gly  
 100 105 110

Phe Leu His Ser Gly Thr Ala Lys Ser Val Thr Cys Thr Tyr Ser Pro  
 115 120 125

Ala Leu Asn Lys Met Phe Cys Gln Leu Ala Lys Thr Cys Pro Val Gln  
 130 135 140

Leu Trp Val Asp Ser Thr Pro Pro Pro Gly Thr Arg Val Arg Ala Met  
 145 150 155 160

Ala Ile Tyr Lys Gln Ser Gln His Met Thr Glu Val Val Arg Arg Cys  
 165 170 175

Pro His His Glu Arg Cys Ser Asp Ser Asp Gly Leu Ala Pro Pro Gln  
 180 185 190

His Leu Ile Arg Val Glu Gly Asn Leu Arg Val Glu Tyr Leu Asp Asp  
 195 200 205

229/299

Arg Asn Thr Phe Arg His Ser Val Val Val Pro Tyr Glu Pro Pro Glu  
 210 215 220  
 Val Gly Ser Asp Cys Thr Thr Ile His Tyr Asn Tyr Met Cys Asn Ser  
 225 230 235 240  
 Ser Cys Met Gly Gly Met Asn Arg Arg Pro Ile Leu Thr Ile Ile Thr  
 245 250 255  
 Leu Glu Asp Ser Ser Gly Asn Leu Leu Gly Arg Asn Ser Phe Glu Val  
 260 265 270  
 Arg Val Cys Ala Cys Pro Gly Arg Asp Arg Arg Thr Glu Glu Glu Asn  
 275 280 285  
 Leu Arg Lys Lys Gly Glu Pro His His Glu Leu Pro Pro Gly Ser Thr  
 290 295 300  
 Lys Arg Ala Leu Pro Asn Asn Thr Ser Ser Ser Pro Gln Pro Lys Lys  
 305 310 315 320  
 Lys Pro Leu Asp Gly Glu Tyr Phe Thr Leu Gln Ile Arg Gly Arg Glu  
 325 330 335  
 Arg Phe Glu Met Phe Arg Glu Leu Asn Glu Ala Leu Glu Leu Lys Asp  
 340 345 350  
 Ala Gln Ala Gly Lys Glu Pro Gly Gly Ser Arg Ala His Ser Ser His  
 355 360 365  
 Leu Lys Ser Lys Lys Gly Gln Ser Thr Ser Arg His Lys Lys Leu Met  
 370 375 380  
 Phe Lys Thr Glu Gly Pro Asp Ser Asp  
 385 390

&lt;210&gt; 279

&lt;211&gt; 1303

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 279

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gtccaggagc aggtagctgc tgggctccgg ggacactttg cgttcgggct gggagcgtgc 60
tttccacgac ggtgacacgc ttccctggat tggcagccag actgccttcc gggtcactgc 120
catggaggag ccgcagtcag atcctagcgt cgagccccct ctgagtcagg aaacattttc 180
agacctatgg aaactacttc ctgaaaacaa cgttctgtcc cccttgccgt cccaagcaat 240
ggatgatttg atgctgtccc cggacgatat tgaacaatgg ttcactgaag acccaggtcc 300
agatgaagct ccagagaatgc cagaggctgc tccccccgtg gcccctgcac cagcgactcc 360
tacaccggcg gcccctgcac cagccccctc ctggccccctg tcatcttctg tcccttccca 420
gaaaacctac cagggcagct acggtttccg tctgggcttc ttgcattctg ggacagccaa 480
gtctgtgact tgcacgtact cccctgccc tcaacaagatg ttttgccaac tggccaagac 540
ctgcocctgtg cagctgtggg ttgattccac acccccgcgc ggcaccgcgc tccgcgccat 600
ggccatctac aagcagtcac agcacatgac ggaggttgtg aggcgctgcc cccaccatga 660
gcgctgctca gatagcgatg gtctggcccc tcctcagcat cttatccgag tgggaaggaaa 720
tttgcggtgtg gagtatattg atgacagaaa cacttttcga catagtgtgg tgggtgccta 780
tgagccgcct gaggttggt ctgactgtac caccatccac tacaactaca tgtgtaacag 840
ttcctgcatg ggcggcatga accggaggcc catcctcacc atcatcacac tgggaagactc 900

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230/299

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cagtggtaat ctactgggac ggaacagctt tgaggtgcgt gtttgtgcct gtcctgggag 960
agaccggcgc acagaggaag agaatctccg caagaaaggg gagcctcacc acgagctgcc 1020
cccaggagag actaagcgag cactgcccac caacaccagc tcctctcccc agccaaagaa 1080
gaaaccactg gatggagaat atttcaccct tcagatccgt gggcgtgagc gcttcgagat 1140
gttccgagag ctgaatgagg ccttggaact caaggatgcc caggctggga aggagccagg 1200
ggggagcagg gctcactcca gccacctgaa gtccaaaag ggtcagtcta cctcccgcc 1260
taaaaaactc atgttcaaga cagaagggcc tgactcagac tga 1303

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&lt;210&gt; 280

&lt;211&gt; 448

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 280

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Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe
  1                      5                      10          15

Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro
          20                      25          30

Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn
          35                      40          45

Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu
          50                      55          60

Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser
          65                      70          75          80

Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn
          85                      90          95

Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln
          100                     105          110

Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser
          115                     120          125

Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln
          130                     135          140

Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys
          145                     150          155          160

Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val
          165                     170          175

Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr
          180                     185          190

Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His
          195                     200          205

Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His
          210                     215          220

Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro

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231/299

225	230	235	240
Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val			
	245	250	255
Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser			
	260	265	270
Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu			
	275	280	285
Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg			
	290	295	300
Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile			
305	310	315	320
Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys			
	325	330	335
Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys			
	340	345	350
Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly			
	355	360	365
Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu			
	370	375	380
Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln			
385	390	395	400
Gln Gln Gln His Gln His Leu Leu Gln Lys His Leu Leu Ser Ala Cys			
	405	410	415
Phe Arg Asn Glu Leu Val Glu Pro Arg Arg Glu Thr Pro Lys Gln Ser			
	420	425	430
Asp Val Phe Phe Arg His Ser Lys Pro Pro Asn Arg Ser Val Tyr Pro			
	435	440	445

&lt;210&gt; 281

&lt;211&gt; 2816

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 281

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tcgttgatat caaagacagt tgaaggaaat gaattttgaa acttcacggt gtgccaccct 60
acagtactgc cctgaccctt acatccagcg tttcgtagaa acccagctca tttctcttgg 120
aaagaaagtt attaccgatc caccatgtcc cagagcacac agacaaatga attcctcagt 180
ccagagggtt tccagcatat ctgggatttt ctggaacagc ctatatgttc agttcagccc 240
attgacttga actttgtgga tgaaccatca gaagatggtg cgacaaacaa gattgagatt 300
agcatggact gtatccgcac gcaggactcg gacctgagtg acccatgtg gccacagtac 360
acgaacctgg ggctcctgaa cagcatggac cagcagattc agaacggctc ctcgtccacc 420
agtccctata acacagacca cgcgcagaac agcgtcacgg cgccctcgcc ctacgcacag 480
cccagctcca ccttcgatgc tctctctcca tcaccgcga tccctccaa caccgactac 540
ccaggcccgc acagtttgcga cgtgtccttc cagcagtcga gcaccgcaa gtccggccacc 600

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232/299

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tggacgtatt ccactgaact gaagaaactc tactgccaaa ttgcaaagac atgccccatc 660
cagatcaagg tgatgacccc acctcctcag ggagctgtta tccgcgccat gcctgtctac 720
aaaaaagctg agcacgtcac ggaggtggtg aagcgggtgcc ccaaccatga gctgagccgt 780
gaattcaacg agggacagat tgcccctcct agtcatttga ttcgagtaga ggggaacagc 840
catgcccagt atgtagaaga tccccatcaca ggaagacaga gtgtgctggt accttatgag 900
ccaccccagg ttggcactga attcacgaca gtcttgtaga atttcatgtg taacagcagt 960
tgtgttggag ggatgaaccg ccgtccaatt ttaatcattg ttactctgga aaccagagat 1020
gggcaagtcc tgggcccagc ctgctttgag gcccgatct gtgcttgccc aggaagagac 1080
aggaaggcgg atgaagatag catcagaaag cagcaagttt cggacagtac aaagaacggt 1140
gatggtacga agcgcctgtt tcgtcagaac acacatggta tccagatgac atccatcaag 1200
aaacgaagat ccccagatga tgaactgtta tacttaccag tgaggggccc tgagacttat 1260
gaaatgctgt tgaagatcaa agagtccctg gaactcatgc agtaccttcc tcagcacaca 1320
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ctttcagcct gcttcaggaa tgagcttggt gagccccgga gagaaactcc aaaacaatct 1440
gacgtcttct ttagacattc caagcccca aaccgatcag tgtaccata gagccctatc 1500
tctatatttt aagtgtgtgt gttgtatttc catgtgtata tgtgagtgtg tgtgtgtgta 1560
tgtgtgtgcg tgtgtatcta gccctcataa acaggacttg aagacacttt ggctcagaga 1620
cccaactgct caaaggcaca aagccactag tgagagaatc ttttgaaggg actcaaacct 1680
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gaaccactgt gtttgtctgt gagctttctg ttgtttcctg ggagggaggg gtcaggtggg 1800
gaaaggggca ttaagatggt tattggaacc cttttctgtc ttcttctggt gtttttctaa 1860
aattcacagg gaagcttttg agcaggtctc aaacttaaga tgtcttttta agaaaaggag 1920
aaaaaagttg ttattgtctg tgcataagta agttgtaggt gactgagaga ctcagtcaga 1980
cccttttaat gctggtcatg taataatatt gcaagtagta agaaacgaag gtgtcaagtg 2040
tactgctggg cagcgaggtg atcattacca aaagtaatca actttgtggg tggagagttc 2100
tttgtgagaa cttgcattat ttgtgtcctc ccctcatgtg taggtagaac atttcttaat 2160
gctgtgtacc tgcctctgcc actgtatggt ggcactgtgt atgctaaagt ttttcttgta 2220
catgaaaccc tggaagacct actacaaaaa aactgttggt tggcccccat agcaggtgaa 2280
ctcattttgt gcttttaata gaaagacaaa tccacccag taatattgcc cttacgtagt 2340
tgttttacct tattcaaagc tcaaaataga atttgaagcc ctctcacaaa atctgtgatt 2400
aatttgctta attagagctt ctatccctca agcctaccta ccataaaacc agccatatta 2460
ctgatactgt tcagtgcatt tagccaggag acttacgttt tgagtaagtg agatccaagc 2520
agacgtgtta aaatcagcac tcctggactg gaaattaaag attgaaaggg tagactactt 2580
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ttaagataat agcataaaga ctttaaaaat gttcctcccc tccatcttcc cacaccagt 2700
caccagcact gtattttctg tcaccaagac aatgatttct tgttattgag gctgttgctt 2760
ttgtggatgt gtgattttaa ttttcaataa acttttgcat cttggtttaa aagaaa 2816

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&lt;210&gt; 282

&lt;211&gt; 641

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 282

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Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe
  1                      5                      10                     15

Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro
      20                      25                      30

Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn
      35                      40                      45

Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu
      50                      55                      60

Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser

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65						70						75						80
Met	Asp	Gln	Gln	Ile	Gln	Asn	Gly	Ser	Ser	Ser	Thr	Ser	Pro	Tyr	Asn			
				85					90					95				
Thr	Asp	His	Ala	Gln	Asn	Ser	Val	Thr	Ala	Pro	Ser	Pro	Tyr	Ala	Gln			
				100					105					110				
Pro	Ser	Ser	Thr	Phe	Asp	Ala	Leu	Ser	Pro	Ser	Pro	Ala	Ile	Pro	Ser			
				115					120					125				
Asn	Thr	Asp	Tyr	Pro	Gly	Pro	His	Ser	Phe	Asp	Val	Ser	Phe	Gln	Gln			
				130					135					140				
Ser	Ser	Thr	Ala	Lys	Ser	Ala	Thr	Trp	Thr	Tyr	Ser	Thr	Glu	Leu	Lys			
145					150					155					160			
Lys	Leu	Tyr	Cys	Gln	Ile	Ala	Lys	Thr	Cys	Pro	Ile	Gln	Ile	Lys	Val			
				165					170					175				
Met	Thr	Pro	Pro	Pro	Gln	Gly	Ala	Val	Ile	Arg	Ala	Met	Pro	Val	Tyr			
				180					185					190				
Lys	Lys	Ala	Glu	His	Val	Thr	Glu	Val	Val	Lys	Arg	Cys	Pro	Asn	His			
				195					200					205				
Glu	Leu	Ser	Arg	Glu	Phe	Asn	Glu	Gly	Gln	Ile	Ala	Pro	Pro	Ser	His			
				210					215					220				
Leu	Ile	Arg	Val	Glu	Gly	Asn	Ser	His	Ala	Gln	Tyr	Val	Glu	Asp	Pro			
225					230					235					240			
Ile	Thr	Gly	Arg	Gln	Ser	Val	Leu	Val	Pro	Tyr	Glu	Pro	Pro	Gln	Val			
				245					250					255				
Gly	Thr	Glu	Phe	Thr	Thr	Val	Leu	Tyr	Asn	Phe	Met	Cys	Asn	Ser	Ser			
				260					265					270				
Cys	Val	Gly	Gly	Met	Asn	Arg	Arg	Pro	Ile	Leu	Ile	Ile	Val	Thr	Leu			
				275					280					285				
Glu	Thr	Arg	Asp	Gly	Gln	Val	Leu	Gly	Arg	Arg	Cys	Phe	Glu	Ala	Arg			
				290					295					300				
Ile	Cys	Ala	Cys	Pro	Gly	Arg	Asp	Arg	Lys	Ala	Asp	Glu	Asp	Ser	Ile			
305					310					315					320			
Arg	Lys	Gln	Gln	Val	Ser	Asp	Ser	Thr	Lys	Asn	Gly	Asp	Gly	Thr	Lys			
				325					330					335				
Arg	Pro	Phe	Arg	Gln	Asn	Thr	His	Gly	Ile	Gln	Met	Thr	Ser	Ile	Lys			
				340					345					350				
Lys	Arg	Arg	Ser	Pro	Asp	Asp	Glu	Leu	Leu	Tyr	Leu	Pro	Val	Arg	Gly			
				355					360					365				
Arg	Glu	Thr	Tyr	Glu	Met	Leu	Leu	Lys	Ile	Lys	Glu	Ser	Leu	Glu	Leu			
				370					375					380				



234/299

Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln  
 385 390 395 400  
 Gln Gln Gln His Gln His Leu Leu Gln Lys Gln Thr Ser Ile Gln Ser  
 405 410 415  
 Pro Ser Ser Tyr Gly Asn Ser Ser Pro Pro Leu Asn Lys Met Asn Ser  
 420 425 430  
 Met Asn Lys Leu Pro Ser Val Ser Gln Leu Ile Asn Pro Gln Gln Arg  
 435 440 445  
 Asn Ala Leu Thr Pro Thr Thr Ile Pro Asp Gly Met Gly Ala Asn Ile  
 450 455 460  
 Pro Met Met Gly Thr His Met Pro Met Ala Gly Asp Met Asn Gly Leu  
 465 470 475 480  
 Ser Pro Thr Gln Ala Leu Pro Pro Pro Leu Ser Met Pro Ser Thr Ser  
 485 490 495  
 His Cys Thr Pro Pro Pro Pro Tyr Pro Thr Asp Cys Ser Ile Val Gly  
 500 505 510  
 Phe Leu Ala Arg Leu Gly Cys Ser Ser Cys Leu Asp Tyr Phe Thr Thr  
 515 520 525  
 Gln Gly Leu Thr Thr Ile Tyr Gln Ile Glu His Tyr Ser Met Asp Asp  
 530 535 540  
 Leu Ala Ser Leu Lys Ile Pro Glu Gln Phe Arg His Ala Ile Trp Lys  
 545 550 555 560  
 Gly Ile Leu Asp His Arg Gln Leu His Glu Phe Ser Ser Pro Ser His  
 565 570 575  
 Leu Leu Arg Thr Pro Ser Ser Ala Ser Thr Val Ser Val Gly Ser Ser  
 580 585 590  
 Glu Thr Arg Gly Glu Arg Val Ile Asp Ala Val Arg Phe Thr Leu Arg  
 595 600 605  
 Gln Thr Ile Ser Phe Pro Pro Arg Asp Glu Trp Asn Asp Phe Asn Phe  
 610 615 620  
 Asp Met Asp Ala Arg Arg Asn Lys Gln Gln Arg Ile Lys Glu Glu Gly  
 625 630 635 640

Glu

&lt;210&gt; 283

&lt;211&gt; 2270

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 283

235/299

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tcgttgatat caaagacagt tgaaggaaat gaattttgaa acttcacggt gtgccaccct 60
acagtactgc cctgaccctt acatccagcg tttcgtagaa acccagctca tttctcttgg 120
aaagaaagtt attaccgatc caccatgtcc cagagcacac agacaaatga attcctcagt 180
ccagaggttt tccagcatat ctgggatttt ctggaacagc ctatatgttc agttcagccc 240
attgacttga actttgtgga tgaaccatca gaagatgggtg cgacaaacaa gattgagatt 300
agcatggact gtatccgcat gcaggactcg gacctgagtg accccatgtg gccacagtac 360
acgaacctgg ggctcctgaa cagcatggac cagcagattc agaacggctc ctcgtccacc 420
agtccctata acacagacca cgcgcagaac agcgtcacgg cgccctcgcc ctacgcacag 480
cccagctcca ccttcgatgc tctctctcca tcaccgcga tccctccaa caccgactac 540
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tggacgtatt cactgaact gaagaaactc tactgccaaa ttgcaaagac atgccccatc 660
cagatcaagg tgatgacccc acctcctcag ggagctgtta tccgcgccat gcctgtctac 720
aaaaaagctg agcacgtcac ggagggtggtg aagcgggtgccc ccaaccatga gctgagccgt 780
gaattcaacg agggacagat tgccctcctt agtcatttga ttcgagtaga ggggaacagc 840
catgcccagt atgtagaaga tcccatcaca ggaagacaga gtgtgctggt accttatgag 900
ccaccccagg ttggcactga attcacgaca gtcttgtaca atttcatgtg taacagcagt 960
tgtgttggag ggatgaaccg ccgtccaatt ttaatcattg ttactctgga aaccagagat 1020
gggcaagtcc tgggccgacg ctgctttgag gcccggtact gtgcttgccc aggaagagac 1080
aggaaggcgg atgaagatag catcagaaaag cagcaagttt cggacagtac aaagaacggt 1140
gatggtacga agcgcgccgtt tcgtcagaac acacatggta tccagatgac atccatcaag 1200
aaacgaagat ccccatgatga tgaactgtta tacttaccag tgaggggccc tgagacttat 1260
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caatttgcag atgcgatctg gaagggcac ctggaccacc ggcagctcca cgaattctcc 1860
tcccttctc atctcctgcg gacccaagc agtcctcta cagtcagtgt gggctccagt 1920
gagacccggg gtgagcgtgt tattgatgct gtgcgattca cctccgcca gaccatctct 1980
ttcccacccc gagatgagtg gaatgacttc aactttgaca tggatgctcg ccgcaataag 2040
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tcctaactgc cagcccccta aaagcactcc tgcttaactt tcaaagcctt ctccctagct 2160
cctcccttc ctcttgtctg atttcttagg ggaaggagaa gtaagaggct acctcttacc 2220
taacatctga cctggcatct aattctgatt ctggctttaa gccttcaaaa 2270

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&lt;210&gt; 284

&lt;211&gt; 471

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 284

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Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe
  1                      5                      10                      15

Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro
      20                      25                      30

Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn
      35                      40                      45

Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu
      50                      55                      60

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236/299

Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser  
 65 70 75 80  
 Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn  
 85 90 95  
 Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln  
 100 105 110  
 Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser  
 115 120 125  
 Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln  
 130 135 140  
 Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys  
 145 150 155 160  
 Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val  
 165 170 175  
 Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr  
 180 185 190  
 Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His  
 195 200 205  
 Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His  
 210 215 220  
 Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro  
 225 230 235 240  
 Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val  
 245 250 255  
 Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser  
 260 265 270  
 Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu  
 275 280 285  
 Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg  
 290 295 300  
 Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile  
 305 310 315 320  
 Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys  
 325 330 335  
 Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys  
 340 345 350  
 Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly  
 355 360 365  
 Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu

237/299

370                                      375                                      380  
 Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln  
 385                                      390                                      395                                      400  
 Gln Gln Gln His Gln His Leu Leu Gln Lys Gln Thr Ser Ile Gln Ser  
                                     405                                      410                                      415  
 Pro Ser Ser Tyr Gly Asn Ser Ser Pro Pro Leu Asn Lys Met Asn Ser  
                                     420                                      425                                      430  
 Met Asn Lys Leu Pro Ser Val Ser Gln Leu Ile Asn Pro Gln Gln Arg  
                                     435                                      440                                      445  
 Asn Ala Leu Thr Pro Thr Thr Ile Pro Asp Gly Met Gly Ala Asn Arg  
                                     450                                      455                                      460  
 Ser Gly Lys Ser Glu Asn Pro  
 465                                      470

&lt;210&gt; 285

&lt;211&gt; 2031

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 285

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tcgttgatat caaagacagt tgaaggaaat gaattttgaa acttcacggg gtgccaccct 60
acagtactgc cctgaccctt acatccagcg ttctcgtaga acccagctca tttctcttgg 120
aaagaaagtt attaccgatc caccatgtcc cagagcacac agacaaatga attcctcagt 180
ccagagggtt tccagcatat ctgggatttt ctggaacagc ctatatgttc agttcagccc 240
attgacttga acttttgtga tgaaccatca gaagatgggt cgacaaacaa gattgagatt 300
agcatggact gtatccgcat gcaggactcg gacctgagtg accccatgtg gccacagtac 360
acgaacctgg ggctcctgaa cagcatggac cagcagattc agaacggctc ctcgtccacc 420
agtccctata acacagacca cgcgcagaac agcgtcacgg cgccctcgcc ctacgcacag 480
cccagctcca ccttcgatgc tctctctcca tcaccgcgca tccctccaa caccgactac 540
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tggacgtatt ccactgaact gaagaaactc tactgccaat ttgcaaagac atgccccatc 660
cagatcaagg tgaatgacccc acctcctcag ggagctgtta tccgcgccat gctgtctac 720
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gaattcaacg agggacagat tgccccctct agtcatttga ttcgagtaga ggggaacagc 840
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tgtgttgagg ggatgaaccg ccgtccaatt ttaatcattg ttactctgga aaccagagat 1020
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gatggtacga agcgcccggt tcgtcagaac acacatggta tccagatgac atccatcaag 1200
aaacgaagat ccccgatga tgaactgtta tacttaccag tgaggggccc tgagacttat 1260
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gcaatttctg catgcatctt ggaagggcat cctggaccac cggcagctcc acgaattctc 1620
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tttccccccc cgagatgagt ggaatgactt caactttgac atggatgctc gccgcaataa 1800
gcaacagcgc atcaaagagg agggggagtg agcctcacca tgtgagctct tcctatccct 1860

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238/299

ctcctaactg ccagccccct aaaagcactc ctgcttaatc ttcaaagcct tctccctagc 1920  
 tcctcccctt cctcttgtct gatttcttag gggaaggaga agtaagaggc tacctcttac 1980  
 ctaacatctg acctggcatt taattctgat tctggcttta agccttcaaa a 2031

&lt;210&gt; 286

&lt;211&gt; 416

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 286

Met	Leu	Tyr	Leu	Glu	Asn	Asn	Ala	Gln	Thr	Gln	Phe	Ser	Glu	Pro	Gln	1	5	10	15
Tyr	Thr	Asn	Leu	Gly	Leu	Leu	Asn	Ser	Met	Asp	Gln	Gln	Ile	Gln	Asn	20	25	30	
Gly	Ser	Ser	Ser	Thr	Ser	Pro	Tyr	Asn	Thr	Asp	His	Ala	Gln	Asn	Ser	35	40	45	
Val	Thr	Ala	Pro	Ser	Pro	Tyr	Ala	Gln	Pro	Ser	Ser	Thr	Phe	Asp	Ala	50	55	60	
Leu	Ser	Pro	Ser	Pro	Ala	Ile	Pro	Ser	Asn	Thr	Asp	Tyr	Pro	Gly	Pro	65	70	75	80
His	Ser	Phe	Asp	Val	Ser	Phe	Gln	Gln	Ser	Ser	Thr	Ala	Lys	Ser	Ala	85	90	95	
Thr	Trp	Thr	Tyr	Ser	Thr	Glu	Leu	Lys	Lys	Leu	Tyr	Cys	Gln	Ile	Ala	100	105	110	
Lys	Thr	Cys	Pro	Ile	Gln	Ile	Lys	Val	Met	Thr	Pro	Pro	Pro	Gln	Gly	115	120	125	
Ala	Val	Ile	Arg	Ala	Met	Pro	Val	Tyr	Lys	Lys	Ala	Glu	His	Val	Thr	130	135	140	
Glu	Val	Val	Lys	Arg	Cys	Pro	Asn	His	Glu	Leu	Ser	Arg	Glu	Phe	Asn	145	150	155	160
Glu	Gly	Gln	Ile	Ala	Pro	Pro	Ser	His	Leu	Ile	Arg	Val	Glu	Gly	Asn	165	170	175	
Ser	His	Ala	Gln	Tyr	Val	Glu	Asp	Pro	Ile	Thr	Gly	Arg	Gln	Ser	Val	180	185	190	
Leu	Val	Pro	Tyr	Glu	Pro	Pro	Gln	Val	Gly	Thr	Glu	Phe	Thr	Thr	Val	195	200	205	
Leu	Tyr	Asn	Phe	Met	Cys	Asn	Ser	Ser	Cys	Val	Gly	Gly	Met	Asn	Arg	210	215	220	
Arg	Pro	Ile	Leu	Ile	Ile	Val	Thr	Leu	Glu	Thr	Arg	Asp	Gly	Gln	Val	225	230	235	240
Leu	Gly	Arg	Arg	Cys	Phe	Glu	Ala	Arg	Ile	Cys	Ala	Cys	Pro	Gly	Arg	245	250	255	

239/299

Asp Arg Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp  
 260 265 270  
 Ser Thr Lys Asn Gly Asp Gly Thr Lys Arg Pro Phe Arg Gln Asn Thr  
 275 280 285  
 His Gly Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp  
 290 295 300  
 Glu Leu Leu Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu  
 305 310 315 320  
 Leu Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His  
 325 330 335  
 Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln His Gln His Leu  
 340 345 350  
 Leu Gln Lys Gln Thr Ser Ile Gln Ser Pro Ser Ser Tyr Gly Asn Ser  
 355 360 365  
 Ser Pro Pro Leu Asn Lys Met Asn Ser Met Asn Lys Leu Pro Ser Val  
 370 375 380  
 Ser Gln Leu Ile Asn Pro Gln Gln Arg Asn Ala Leu Thr Pro Thr Thr  
 385 390 395 400  
 Ile Pro Asp Gly Met Gly Ala Asn Arg Ser Gly Lys Ser Glu Asn Pro  
 405 410 415

&lt;210&gt; 287

&lt;400&gt; 287

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&lt;210&gt; 288

&lt;211&gt; 461

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 288

Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln  
 1 5 10 15  
 Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn  
 20 25 30  
 Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser  
 35 40 45  
 Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala  
 50 55 60  
 Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro  
 65 70 75 80

240/299

His	Ser	Phe	Asp	Val	Ser	Phe	Gln	Gln	Ser	Ser	Thr	Ala	Lys	Ser	Ala	85	90	95
Thr	Trp	Thr	Tyr	Ser	Thr	Glu	Leu	Lys	Lys	Leu	Tyr	Cys	Gln	Ile	Ala	100	105	110
Lys	Thr	Cys	Pro	Ile	Gln	Ile	Lys	Val	Met	Thr	Pro	Pro	Pro	Gln	Gly	115	120	125
Ala	Val	Ile	Arg	Ala	Met	Pro	Val	Tyr	Lys	Lys	Ala	Glu	His	Val	Thr	130	135	140
Glu	Val	Val	Lys	Arg	Cys	Pro	Asn	His	Glu	Leu	Ser	Arg	Glu	Phe	Asn	145	150	155
Glu	Gly	Gln	Ile	Ala	Pro	Pro	Ser	His	Leu	Ile	Arg	Val	Glu	Gly	Asn	165	170	175
Ser	His	Ala	Gln	Tyr	Val	Glu	Asp	Pro	Ile	Thr	Gly	Arg	Gln	Ser	Val	180	185	190
Leu	Val	Pro	Tyr	Glu	Pro	Pro	Gln	Val	Gly	Thr	Glu	Phe	Thr	Thr	Val	195	200	205
Leu	Tyr	Asn	Phe	Met	Cys	Asn	Ser	Ser	Cys	Val	Gly	Gly	Met	Asn	Arg	210	215	220
Arg	Pro	Ile	Leu	Ile	Ile	Val	Thr	Leu	Glu	Thr	Arg	Asp	Gly	Gln	Val	225	230	235
Leu	Gly	Arg	Arg	Cys	Phe	Glu	Ala	Arg	Ile	Cys	Ala	Cys	Pro	Gly	Arg	245	250	255
Asp	Arg	Lys	Ala	Asp	Glu	Asp	Ser	Ile	Arg	Lys	Gln	Gln	Val	Ser	Asp	260	265	270
Ser	Thr	Lys	Asn	Gly	Asp	Gly	Thr	Lys	Arg	Pro	Phe	Arg	Gln	Asn	Thr	275	280	285
His	Gly	Ile	Gln	Met	Thr	Ser	Ile	Lys	Lys	Arg	Arg	Ser	Pro	Asp	Asp	290	295	300
Glu	Leu	Leu	Tyr	Leu	Pro	Val	Arg	Gly	Arg	Glu	Thr	Tyr	Glu	Met	Leu	305	310	315
Leu	Lys	Ile	Lys	Glu	Ser	Leu	Glu	Leu	Met	Gln	Tyr	Leu	Pro	Gln	His	325	330	335
Thr	Ile	Glu	Thr	Tyr	Arg	Gln	Gln	Gln	Gln	Gln	Gln	His	Gln	His	Leu	340	345	350
Leu	Gln	Lys	Gln	Thr	Ser	Ile	Gln	Ser	Pro	Ser	Ser	Tyr	Gly	Asn	Ser	355	360	365
Ser	Pro	Pro	Leu	Asn	Lys	Met	Asn	Ser	Met	Asn	Lys	Leu	Pro	Ser	Val	370	375	380

241/299

Ser Gln Leu Ile Asn Pro Gln Gln Arg Asn Ala Leu Thr Pro Thr Thr  
 385 390 395 400

Ile Pro Asp Gly Met Gly Ala Asn Ile Pro Met Met Gly Thr His Met  
 405 410 415

Pro Met Ala Gly Asp Met Asn Gly Leu Ser Pro Thr Gln Ala Leu Pro  
 420 425 430

Pro Pro Leu Ser Met Pro Ser Thr Ser His Cys Thr Pro Pro Pro Pro  
 435 440 445

Tyr Pro Thr Asp Cys Ser Ile Val Gly Ile Trp Gln Val  
 450 455 460

&lt;210&gt; 289

<400> 289  
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&lt;210&gt; 290

&lt;211&gt; 586

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 290

Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln  
 1 5 10 15

Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn  
 20 25 30

Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser  
 35 40 45

Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala  
 50 55 60

Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro  
 65 70 75 80

His Ser Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala  
 85 90 95

Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala  
 100 105 110

Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly  
 115 120 125

Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr  
 130 135 140

Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn  
 145 150 155 160



242/299

Glu	Gly	Gln	Ile	Ala	Pro	Pro	Ser	His	Leu	Ile	Arg	Val	Glu	Gly	Asn		
				165					170					175			
Ser	His	Ala	Gln	Tyr	Val	Glu	Asp	Pro	Ile	Thr	Gly	Arg	Gln	Ser	Val		
			180					185					190				
Leu	Val	Pro	Tyr	Glu	Pro	Pro	Gln	Val	Gly	Thr	Glu	Phe	Thr	Thr	Val		
		195					200					205					
Leu	Tyr	Asn	Phe	Met	Cys	Asn	Ser	Ser	Cys	Val	Gly	Gly	Met	Asn	Arg		
	210					215					220						
Arg	Pro	Ile	Leu	Ile	Ile	Val	Thr	Leu	Glu	Thr	Arg	Asp	Gly	Gln	Val		
225					230					235					240		
Leu	Gly	Arg	Arg	Cys	Phe	Glu	Ala	Arg	Ile	Cys	Ala	Cys	Pro	Gly	Arg		
				245					250					255			
Asp	Arg	Lys	Ala	Asp	Glu	Asp	Ser	Ile	Arg	Lys	Gln	Gln	Val	Ser	Asp		
			260					265					270				
Ser	Thr	Lys	Asn	Gly	Asp	Gly	Thr	Lys	Arg	Pro	Phe	Arg	Gln	Asn	Thr		
		275					280					285					
His	Gly	Ile	Gln	Met	Thr	Ser	Ile	Lys	Lys	Arg	Arg	Ser	Pro	Asp	Asp		
	290					295					300						
Glu	Leu	Leu	Tyr	Leu	Pro	Val	Arg	Gly	Arg	Glu	Thr	Tyr	Glu	Met	Leu		
305					310					315					320		
Leu	Lys	Ile	Lys	Glu	Ser	Leu	Glu	Leu	Met	Gln	Tyr	Leu	Pro	Gln	His		
				325					330					335			
Thr	Ile	Glu	Thr	Tyr	Arg	Gln	Gln	Gln	Gln	Gln	Gln	His	Gln	His	Leu		
			340					345					350				
Leu	Gln	Lys	Gln	Thr	Ser	Ile	Gln	Ser	Pro	Ser	Ser	Tyr	Gly	Asn	Ser		
	355						360					365					
Ser	Pro	Pro	Leu	Asn	Lys	Met	Asn	Ser	Met	Asn	Lys	Leu	Pro	Ser	Val		
	370					375					380						
Ser	Gln	Leu	Ile	Asn	Pro	Gln	Gln	Arg	Asn	Ala	Leu	Thr	Pro	Thr	Thr		
385				390						395					400		
Ile	Pro	Asp	Gly	Met	Gly	Ala	Asn	Ile	Pro	Met	Met	Gly	Thr	His	Met		
				405					410					415			
Pro	Met	Ala	Gly	Asp	Met	Asn	Gly	Leu	Ser	Pro	Thr	Gln	Ala	Leu	Pro		
			420					425					430				
Pro	Pro	Leu	Ser	Met	Pro	Ser	Thr	Ser	His	Cys	Thr	Pro	Pro	Pro	Pro		
			435				440					445					
Tyr	Pro	Thr	Asp	Cys	Ser	Ile	Val	Gly	Phe	Leu	Ala	Arg	Leu	Gly	Cys		
	450					455					460						
Ser	Ser	Cys	Leu	Asp	Tyr	Phe	Thr	Thr	Gln	Gly	Leu	Thr	Thr	Ile	Tyr		

243/299

465                      470                      475                      480  
 Gln Ile Glu His Tyr Ser Met Asp Asp Leu Ala Ser Leu Lys Ile Pro  
                                  485                      490                      495  
 Glu Gln Phe Arg His Ala Ile Trp Lys Gly Ile Leu Asp His Arg Gln  
                                  500                      505                      510  
 Leu His Glu Phe Ser Ser Pro Ser His Leu Leu Arg Thr Pro Ser Ser  
                                  515                      520                      525  
 Ala Ser Thr Val Ser Val Gly Ser Ser Glu Thr Arg Gly Glu Arg Val  
                                  530                      535                      540  
 Ile Asp Ala Val Arg Phe Thr Leu Arg Gln Thr Ile Ser Phe Pro Pro  
 545                                   550                      555                      560  
 Arg Asp Glu Trp Asn Asp Phe Asn Phe Asp Met Asp Ala Arg Arg Asn  
                                  565                      570                      575  
 Lys Gln Gln Arg Ile Lys Glu Glu Gly Glu  
                                  580                      585

&lt;210&gt; 291

&lt;400&gt; 291

000

&lt;210&gt; 292

&lt;211&gt; 393

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 292

Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln  
   1                                 5                                 10                                 15  
 Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn  
                                  20                                 25                                 30  
 Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser  
                                  35                                 40                                 45  
 Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala  
                                  50                                 55                                 60  
 Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro  
 65                                 70                                 75                                 80  
 His Ser Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala  
                                  85                                 90                                 95  
 Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala  
                                  100                                 105                                 110  
 Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly

244/299

115					120					125					
Ala	Val	Ile	Arg	Ala	Met	Pro	Val	Tyr	Lys	Lys	Ala	Glu	His	Val	Thr
130					135					140					
Glu	Val	Val	Lys	Arg	Cys	Pro	Asn	His	Glu	Leu	Ser	Arg	Glu	Phe	Asn
145					150					155					160
Glu	Gly	Gln	Ile	Ala	Pro	Pro	Ser	His	Leu	Ile	Arg	Val	Glu	Gly	Asn
				165					170					175	
Ser	His	Ala	Gln	Tyr	Val	Glu	Asp	Pro	Ile	Thr	Gly	Arg	Gln	Ser	Val
			180					185					190		
Leu	Val	Pro	Tyr	Glu	Pro	Pro	Gln	Val	Gly	Thr	Glu	Phe	Thr	Thr	Val
		195					200					205			
Leu	Tyr	Asn	Phe	Met	Cys	Asn	Ser	Ser	Cys	Val	Gly	Gly	Met	Asn	Arg
	210					215					220				
Arg	Pro	Ile	Leu	Ile	Ile	Val	Thr	Leu	Glu	Thr	Arg	Asp	Gly	Gln	Val
225						230					235				240
Leu	Gly	Arg	Arg	Cys	Phe	Glu	Ala	Arg	Ile	Cys	Ala	Cys	Pro	Gly	Arg
				245					250					255	
Asp	Arg	Lys	Ala	Asp	Glu	Asp	Ser	Ile	Arg	Lys	Gln	Gln	Val	Ser	Asp
			260					265					270		
Ser	Thr	Lys	Asn	Gly	Asp	Gly	Thr	Lys	Arg	Pro	Phe	Arg	Gln	Asn	Thr
		275					280					285			
His	Gly	Ile	Gln	Met	Thr	Ser	Ile	Lys	Lys	Arg	Arg	Ser	Pro	Asp	Asp
	290					295					300				
Glu	Leu	Leu	Tyr	Leu	Pro	Val	Arg	Gly	Arg	Glu	Thr	Tyr	Glu	Met	Leu
305						310					315				320
Leu	Lys	Ile	Lys	Glu	Ser	Leu	Glu	Leu	Met	Gln	Tyr	Leu	Pro	Gln	His
				325					330					335	
Thr	Ile	Glu	Thr	Tyr	Arg	Gln	Gln	Gln	Gln	Gln	Gln	His	Gln	His	Leu
			340					345					350		
Leu	Gln	Lys	His	Leu	Leu	Ser	Ala	Cys	Phe	Arg	Asn	Glu	Leu	Val	Glu
		355					360					365			
Pro	Arg	Arg	Glu	Thr	Pro	Lys	Gln	Ser	Asp	Val	Phe	Phe	Arg	His	Ser
			370				375					380			
Lys	Pro	Pro	Asn	Arg	Ser	Val	Tyr	Pro							
385						390									

&lt;210&gt; 293

&lt;400&gt; 293

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245/299

&lt;210&gt; 294

&lt;211&gt; 471

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 294

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Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe
 1           5           10           15

Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro
          20           25           30

Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn
          35           40           45

Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu
 50           55           60

Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser
 65           70           75           80

Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn
          85           90           95

Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln
          100          105          110

Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser
          115          120          125

Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln
          130          135          140

Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys
          145          150          155          160

Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val
          165          170          175

Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr
          180          185          190

Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His
          195          200          205

Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His
          210          215          220

Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro
          225          230          235          240

Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val
          245          250          255

Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser
          260          265          270

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Cys	Val	Gly 275	Gly	Met	Asn	Arg	Arg 280	Pro	Ile	Leu	Ile	Ile 285	Val	Thr	Leu
Glu	Thr 290	Arg	Asp	Gly	Gln	Val 295	Leu	Gly	Arg	Arg	Cys 300	Phe	Glu	Ala	Arg
Ile 305	Cys	Ala	Cys	Pro	Gly 310	Arg	Asp	Arg	Lys	Ala 315	Asp	Glu	Asp	Ser	Ile 320
Arg	Lys	Gln	Gln	Val 325	Ser	Asp	Ser	Thr	Lys 330	Asn	Gly	Asp	Gly	Thr 335	Lys
Arg	Pro	Phe 340	Arg	Gln	Asn	Thr	His	Gly 345	Ile	Gln	Met	Thr 350	Ser	Ile	Lys
Lys	Arg	Arg 355	Ser	Pro	Asp	Asp	Glu 360	Leu	Leu	Tyr	Leu	Pro 365	Val	Arg	Gly
Arg	Glu 370	Thr	Tyr	Glu	Met	Leu 375	Leu	Lys	Ile	Lys	Glu 380	Ser	Leu	Glu	Leu
Met 385	Gln	Tyr	Leu	Pro	Gln 390	His	Thr	Ile	Glu	Thr 395	Tyr	Arg	Gln	Gln	Gln 400
Gln	Gln	Gln	His	Gln 405	His	Leu	Leu	Gln	Lys 410	Gln	Thr	Ser	Ile	Gln 415	Ser
Pro	Ser	Ser 420	Tyr	Gly	Asn	Ser	Ser	Pro 425	Pro	Leu	Asn	Lys 430	Met	Asn	Ser
Met	Asn 435	Lys	Leu	Pro	Ser	Val	Ser 440	Gln	Leu	Ile	Asn	Pro 445	Gln	Gln	Arg
Asn	Ala 450	Leu	Thr	Pro	Thr	Thr 455	Ile	Pro	Asp	Gly	Met 460	Gly	Ala	Asn	Arg
Ser 465	Gly	Lys	Ser	Glu	Asn 470	Pro									

Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro  
20 25 30

247/299

Ile	Asp	Leu	Asn	Phe	Val	Asp	Glu	Pro	Ser	Glu	Asp	Gly	Ala	Thr	Asn
		35					40					45			
Lys	Ile	Glu	Ile	Ser	Met	Asp	Cys	Ile	Arg	Met	Gln	Asp	Ser	Asp	Leu
	50					55					60				
Ser	Asp	Pro	Met	Trp	Pro	Gln	Tyr	Thr	Asn	Leu	Gly	Leu	Leu	Asn	Ser
65					70					75					80
Met	Asp	Gln	Gln	Ile	Gln	Asn	Gly	Ser	Ser	Ser	Thr	Ser	Pro	Tyr	Asn
				85					90					95	
Thr	Asp	His	Ala	Gln	Asn	Ser	Val	Thr	Ala	Pro	Ser	Pro	Tyr	Ala	Gln
			100					105					110		
Pro	Ser	Ser	Thr	Phe	Asp	Ala	Leu	Ser	Pro	Ser	Pro	Ala	Ile	Pro	Ser
		115					120					125			
Asn	Thr	Asp	Tyr	Pro	Gly	Pro	His	Ser	Phe	Asp	Val	Ser	Phe	Gln	Gln
	130					135					140				
Ser	Ser	Thr	Ala	Lys	Ser	Ala	Thr	Trp	Thr	Tyr	Ser	Thr	Glu	Leu	Lys
145					150					155					160
Lys	Leu	Tyr	Cys	Gln	Ile	Ala	Lys	Thr	Cys	Pro	Ile	Gln	Ile	Lys	Val
				165					170					175	
Met	Thr	Pro	Pro	Pro	Gln	Gly	Ala	Val	Ile	Arg	Ala	Met	Pro	Val	Tyr
			180					185					190		
Lys	Lys	Ala	Glu	His	Val	Thr	Glu	Val	Val	Lys	Arg	Cys	Pro	Asn	His
		195					200					205			
Glu	Leu	Ser	Arg	Glu	Phe	Asn	Glu	Gly	Gln	Ile	Ala	Pro	Pro	Ser	His
						215					220				
Leu	Ile	Arg	Val	Glu	Gly	Asn	Ser	His	Ala	Gln	Tyr	Val	Glu	Asp	Pro
225					230					235					240
Ile	Thr	Gly	Arg	Gln	Ser	Val	Leu	Val	Pro	Tyr	Glu	Pro	Pro	Gln	Val
				245					250					255	
Gly	Thr	Glu	Phe	Thr	Thr	Val	Leu	Tyr	Asn	Phe	Met	Cys	Asn	Ser	Ser
			260					265					270		
Cys	Val	Gly	Gly	Met	Asn	Arg	Arg	Pro	Ile	Leu	Ile	Ile	Val	Thr	Leu
		275					280					285			
Glu	Thr	Arg	Asp	Gly	Gln	Val	Leu	Gly	Arg	Arg	Cys	Phe	Glu	Ala	Arg
		290				295					300				
Ile	Cys	Ala	Cys	Pro	Gly	Arg	Asp	Arg	Lys	Ala	Asp	Glu	Asp	Ser	Ile
305					310					315					320
Arg	Lys	Gln	Gln	Val	Ser	Asp	Ser	Thr	Lys	Asn	Gly	Asp	Gly	Thr	Lys
				325					330					335	

248/299

Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys  
 340 345 350  
 Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly  
 355 360 365  
 Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu  
 370 375 380  
 Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln  
 385 390 395 400  
 Gln Gln Gln His Gln His Leu Leu Gln Lys Gln Thr Ser Ile Gln Ser  
 405 410 415  
 Pro Ser Ser Tyr Gly Asn Ser Ser Pro Pro Leu Asn Lys Met Asn Ser  
 420 425 430  
 Met Asn Lys Leu Pro Ser Val Ser Gln Leu Ile Asn Pro Gln Gln Arg  
 435 440 445  
 Asn Ala Leu Thr Pro Thr Thr Ile Pro Asp Gly Met Gly Ala Asn Ile  
 450 455 460  
 Pro Met Met Gly Thr His Met Pro Met Ala Gly Asp Met Asn Gly Leu  
 465 470 475 480  
 Ser Pro Thr Gln Ala Leu Pro Pro Pro Leu Ser Met Pro Ser Thr Ser  
 485 490 495  
 His Cys Thr Pro Pro Pro Pro Tyr Pro Thr Asp Cys Ser Ile Val Gly  
 500 505 510  
 Ile Trp Gln Val  
 515

&lt;210&gt; 297

&lt;400&gt; 297

000

&lt;210&gt; 298

&lt;211&gt; 641

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 298

Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe  
 1 5 10 15  
 Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro  
 20 25 30  
 Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn  
 35 40 45

249/299

Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu  
 50 55 60  
 Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser  
 65 70 75 80  
 Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn  
 85 90 95  
 Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln  
 100 105 110  
 Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser  
 115 120 125  
 Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln  
 130 135 140  
 Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys  
 145 150 155 160  
 Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val  
 165 170 175  
 Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr  
 180 185 190  
 Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His  
 195 200 205  
 Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His  
 210 215 220  
 Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro  
 225 230 235 240  
 Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val  
 245 250 255  
 Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser  
 260 265 270  
 Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu  
 275 280 285  
 Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg  
 290 295 300  
 Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile  
 305 310 315 320  
 Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys  
 325 330 335  
 Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys  
 340 345 350  
 Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly



250/299

355	360	365
Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu		
370	375	380
Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln		
385	390	395
Gln Gln Gln His Gln His Leu Leu Gln Lys Gln Thr Ser Ile Gln Ser		
405	410	415
Pro Ser Ser Tyr Gly Asn Ser Ser Pro Pro Leu Asn Lys Met Asn Ser		
420	425	430
Met Asn Lys Leu Pro Ser Val Ser Gln Leu Ile Asn Pro Gln Gln Arg		
435	440	445
Asn Ala Leu Thr Pro Thr Thr Ile Pro Asp Gly Met Gly Ala Asn Ile		
450	455	460
Pro Met Met Gly Thr His Met Pro Met Ala Gly Asp Met Asn Gly Leu		
465	470	475
Ser Pro Thr Gln Ala Leu Pro Pro Pro Leu Ser Met Pro Ser Thr Ser		
485	490	495
His Cys Thr Pro Pro Pro Pro Tyr Pro Thr Asp Cys Ser Ile Val Gly		
500	505	510
Phe Leu Ala Arg Leu Gly Cys Ser Ser Cys Leu Asp Tyr Phe Thr Thr		
515	520	525
Gln Gly Leu Thr Thr Ile Tyr Gln Ile Glu His Tyr Ser Met Asp Asp		
530	535	540
Leu Ala Ser Leu Lys Ile Pro Glu Gln Phe Arg His Ala Ile Trp Lys		
545	550	555
Gly Ile Leu Asp His Arg Gln Leu His Glu Phe Ser Ser Pro Ser His		
565	570	575
Leu Leu Arg Thr Pro Ser Ser Ala Ser Thr Val Ser Val Gly Ser Ser		
580	585	590
Glu Thr Arg Gly Glu Arg Val Ile Asp Ala Val Arg Phe Thr Leu Arg		
595	600	605
Gln Thr Ile Ser Phe Pro Pro Arg Asp Glu Trp Asn Asp Phe Asn Phe		
610	615	620
Asp Met Asp Ala Arg Arg Asn Lys Gln Gln Arg Ile Lys Glu Glu Gly		
625	630	635
Glu		

&lt;210&gt; 299

251/299

<400> 299  
000

<210> 300  
<211> 448  
<212> PRT  
<213> Homo sapiens

<400> 300

Met	Ser	Gln	Ser	Thr	Gln	Thr	Asn	Glu	Phe	Leu	Ser	Pro	Glu	Val	Phe
1				5					10					15	
Gln	His	Ile	Trp	Asp	Phe	Leu	Glu	Gln	Pro	Ile	Cys	Ser	Val	Gln	Pro
			20					25					30		
Ile	Asp	Leu	Asn	Phe	Val	Asp	Glu	Pro	Ser	Glu	Asp	Gly	Ala	Thr	Asn
		35					40					45			
Lys	Ile	Glu	Ile	Ser	Met	Asp	Cys	Ile	Arg	Met	Gln	Asp	Ser	Asp	Leu
	50					55					60				
Ser	Asp	Pro	Met	Trp	Pro	Gln	Tyr	Thr	Asn	Leu	Gly	Leu	Leu	Asn	Ser
	65				70					75					80
Met	Asp	Gln	Gln	Ile	Gln	Asn	Gly	Ser	Ser	Ser	Thr	Ser	Pro	Tyr	Asn
				85					90					95	
Thr	Asp	His	Ala	Gln	Asn	Ser	Val	Thr	Ala	Pro	Ser	Pro	Tyr	Ala	Gln
			100					105					110		
Pro	Ser	Ser	Thr	Phe	Asp	Ala	Leu	Ser	Pro	Ser	Pro	Ala	Ile	Pro	Ser
		115					120					125			
Asn	Thr	Asp	Tyr	Pro	Gly	Pro	His	Ser	Phe	Asp	Val	Ser	Phe	Gln	Gln
	130					135					140				
Ser	Ser	Thr	Ala	Lys	Ser	Ala	Thr	Trp	Thr	Tyr	Ser	Thr	Glu	Leu	Lys
145					150					155					160
Lys	Leu	Tyr	Cys	Gln	Ile	Ala	Lys	Thr	Cys	Pro	Ile	Gln	Ile	Lys	Val
			165						170					175	
Met	Thr	Pro	Pro	Pro	Gln	Gly	Ala	Val	Ile	Arg	Ala	Met	Pro	Val	Tyr
			180					185					190		
Lys	Lys	Ala	Glu	His	Val	Thr	Glu	Val	Val	Lys	Arg	Cys	Pro	Asn	His
		195					200					205			
Glu	Leu	Ser	Arg	Glu	Phe	Asn	Glu	Gly	Gln	Ile	Ala	Pro	Pro	Ser	His
	210					215					220				
Leu	Ile	Arg	Val	Glu	Gly	Asn	Ser	His	Ala	Gln	Tyr	Val	Glu	Asp	Pro
225					230					235					240
Ile	Thr	Gly	Arg	Gln	Ser	Val	Leu	Val	Pro	Tyr	Glu	Pro	Pro	Gln	Val
				245					250					255	

252/299

Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser  
                   260                                  265                                  270  
 Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu  
                   275                                  280                                  285  
 Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg  
                   290                                  295                                  300  
 Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile  
 305                                  310                                  315                                  320  
 Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys  
                                   325                                  330                                  335  
 Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys  
                                   340                                  345                                  350  
 Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly  
                                   355                                  360                                  365  
 Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu  
                   370                                  375                                  380  
 Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln  
 385                                  390                                  395                                  400  
 Gln Gln Gln His Gln His Leu Leu Gln Lys His Leu Leu Ser Ala Cys  
                                   405                                  410                                  415  
 Phe Arg Asn Glu Leu Val Glu Pro Arg Arg Glu Thr Pro Lys Gln Ser  
                   420                                  425                                  430  
 Asp Val Phe Phe Arg His Ser Lys Pro Pro Asn Arg Ser Val Tyr Pro  
                   435                                  440                                  445

&lt;210&gt; 301

<400> 301  
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&lt;210&gt; 302

&lt;211&gt; 461

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 302

Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln  
   1                                  5                                  10                                  15  
 Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn  
                   20                                  25                                  30  
 Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser  
                   35                                  40                                  45

253/299

Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala  
 50 55 60  
 Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro  
 65 70 75 80  
 His Ser Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala  
 85 90 95  
 Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala  
 100 105 110  
 Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly  
 115 120 125  
 Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr  
 130 135 140  
 Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn  
 145 150 155 160  
 Glu Gly Gln Ile Ala Pro Pro Ser His Leu Ile Arg Val Glu Gly Asn  
 165 170 175  
 Ser His Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val  
 180 185 190  
 Leu Val Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Val  
 195 200 205  
 Leu Tyr Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg  
 210 215 220  
 Arg Pro Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val  
 225 230 235 240  
 Leu Gly Arg Arg Cys Phe Glu Ala Arg Ile Cys Ala Cys Pro Gly Arg  
 245 250 255  
 Asp Arg Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp  
 260 265 270  
 Ser Thr Lys Asn Gly Asp Gly Thr Lys Arg Pro Phe Arg Gln Asn Thr  
 275 280 285  
 His Gly Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp  
 290 295 300  
 Glu Leu Leu Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu  
 305 310 315 320  
 Leu Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His  
 325 330 335  
 Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln His Gln His Leu  
 340 345 350  
 Leu Gln Lys Gln Thr Ser Ile Gln Ser Pro Ser Ser Tyr Gly Asn Ser

254/299

355		360		365
Ser Pro Pro Leu Asn Lys Met Asn Ser Met Asn Lys Leu Pro Ser Val				
370		375		380
Ser Gln Leu Ile Asn Pro Gln Gln Arg Asn Ala Leu Thr Pro Thr Thr				
385		390		395
Ile Pro Asp Gly Met Gly Ala Asn Ile Pro Met Met Gly Thr His Met				
	405		410	415
Pro Met Ala Gly Asp Met Asn Gly Leu Ser Pro Thr Gln Ala Leu Pro				
	420		425	430
Pro Pro Leu Ser Met Pro Ser Thr Ser His Cys Thr Pro Pro Pro Pro				
	435		440	445
Tyr Pro Thr Asp Cys Ser Ile Val Arg Ile Trp Gln Val				
450		455		460

&lt;210&gt; 303

&lt;211&gt; 1386

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 303

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atgttgtagc tggaaaacaa tgcccagact caatttagtg agccacagta cacgaacctg 60
gggctcctga acagcatgga ccagcagatt cagaacggct cctcgtccac cagtccttat 120
aacacagacc acgcgagaa cagcgtcacg gcgcccctcg cctacgcaca gccagctcc 180
accttcgatg ctctctctcc atcaccgcgc atcccctcca acaccgacta cccaggcccg 240
cacagtgttc acgtgtcctt ccagcagtcg agcaccgcca agtcggccac ctggacgtat 300
tccactgaac tgaagaaact ctactgccaa attgcaaaga catgccccat ccagatcaag 360
gtgatgaccc cacctcctca gggagctgtt atccgcgcca tgcctgtcta caaaaaagct 420
gagcacgtca cggaggtggt gaagcgggtg cccaaccatg agctgagccg tgaattcaac 480
gaggacaga ttgcccctcc tagtcatttg attcgagtag aggggaacag ccatgcccag 540
tatgtagaag atcccatcac aggaagacag agtgtgtgtg taccttatga gccaccccag 600
gttggcactg aattcacgac agtcttgtac aatttcatgt gtaacagcag ttgtgttga 660
gggatgaacc gccgtccaat tttaatcatt gttactctgg aaaccagaga tgggcaagtc 720
ctgggcccga gctgctttga ggcccggatc tgtgcttgcc caggaagaga caggaaggcg 780
gatgaagata gcatcagaaa gcagcaagtt tcggacagta caaagaacgg tgatggtacg 840
aagcgcctgt ttcgtcagaa cacacatggt atccagatga catccatcaa gaaacgaaga 900
tccccagatg atgaactgtt atacttacca gtgagggggc gtgagactta tgaaatgctg 960
ttgaagatca aagagtcctt ggaactcatg cagtaccctc ctcagcacac aattgaaacg 1020
tacaggcaac agcaacagca gcagcaccag cacttacttc agaaacagac ctcaatacag 1080
tctccatctt catatggtaa cagctcccca cctctgaaca aaatgaacag catgaacaag 1140
ctgccttctg tgagccagct tatcaaccct cagcagcgca acgcccctac tcctacaacc 1200
attcctgatg gcatgggagc caacattccc atgatgggca cccacatgcc aatggctgga 1260
gacatgaatg gactcagccc caccaggga ctcctctccc cactctccat gccatccacc 1320
tcccactgca cacccccacc tccgtatccc acagattgca gcattgtcag gatctggcaa 1380
gtctga                                     1386

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&lt;210&gt; 304

&lt;211&gt; 393

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

255/299

&lt;400&gt; 304

Met	Leu	Tyr	Leu	Glu	Asn	Asn	Ala	Gln	Thr	Gln	Phe	Ser	Glu	Pro	Gln	1	5	10	15
Tyr	Thr	Asn	Leu	Gly	Leu	Leu	Asn	Ser	Met	Asp	Gln	Gln	Ile	Gln	Asn	20	25	30	
Gly	Ser	Ser	Ser	Thr	Ser	Pro	Tyr	Asn	Thr	Asp	His	Ala	Gln	Asn	Ser	35	40	45	
Val	Thr	Ala	Pro	Ser	Pro	Tyr	Ala	Gln	Pro	Ser	Ser	Thr	Phe	Asp	Ala	50	55	60	
Leu	Ser	Pro	Ser	Pro	Ala	Ile	Pro	Ser	Asn	Thr	Asp	Tyr	Pro	Gly	Pro	65	70	75	80
His	Ser	Phe	Asp	Val	Ser	Phe	Gln	Gln	Ser	Ser	Thr	Ala	Lys	Ser	Ala	85	90	95	
Thr	Trp	Thr	Tyr	Ser	Thr	Glu	Leu	Lys	Lys	Leu	Tyr	Cys	Gln	Ile	Ala	100	105	110	
Lys	Thr	Cys	Pro	Ile	Gln	Ile	Lys	Val	Met	Thr	Pro	Pro	Pro	Gln	Gly	115	120	125	
Ala	Val	Ile	Arg	Ala	Met	Pro	Val	Tyr	Lys	Lys	Ala	Glu	His	Val	Thr	130	135	140	
Glu	Val	Val	Lys	Arg	Cys	Pro	Asn	His	Glu	Leu	Ser	Arg	Glu	Phe	Asn	145	150	155	160
Glu	Gly	Gln	Ile	Ala	Pro	Pro	Ser	His	Leu	Ile	Arg	Val	Glu	Gly	Asn	165	170	175	
Ser	His	Ala	Gln	Tyr	Val	Glu	Asp	Pro	Ile	Thr	Gly	Arg	Gln	Ser	Val	180	185	190	
Leu	Val	Pro	Tyr	Glu	Pro	Pro	Gln	Val	Gly	Thr	Glu	Phe	Thr	Thr	Val	195	200	205	
Leu	Tyr	Asn	Phe	Met	Cys	Asn	Ser	Ser	Cys	Val	Gly	Gly	Met	Asn	Arg	210	215	220	
Arg	Pro	Ile	Leu	Ile	Ile	Val	Thr	Leu	Glu	Thr	Arg	Asp	Gly	Gln	Val	225	230	235	240
Leu	Gly	Arg	Arg	Cys	Phe	Glu	Ala	Arg	Ile	Cys	Ala	Cys	Pro	Gly	Arg	245	250	255	
Asp	Arg	Lys	Ala	Asp	Glu	Asp	Ser	Ile	Arg	Lys	Gln	Gln	Val	Ser	Asp	260	265	270	
Ser	Thr	Lys	Asn	Gly	Asp	Gly	Thr	Lys	Arg	Pro	Phe	Arg	Gln	Asn	Thr	275	280	285	
His	Gly	Ile	Gln	Met	Thr	Ser	Ile	Lys	Lys	Arg	Arg	Ser	Pro	Asp	Asp	290	295	300	

256/299

Glu Leu Leu Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu  
 305 310 315 320  
 Leu Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His  
 325 330 335  
 Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln His Gln His Leu  
 340 345 350  
 Leu Gln Lys His Leu Leu Ser Ala Cys Phe Arg Asn Glu Leu Val Glu  
 355 360 365  
 Pro Arg Arg Glu Thr Pro Lys Gln Ser Asp Val Phe Phe Arg His Ser  
 370 375 380  
 Lys Pro Pro Asn Arg Ser Val Tyr Pro  
 385 390

&lt;210&gt; 305

&lt;211&gt; 1182

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 305

```

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aacacagacc acgcgcagaa cagcgtcagc gcgcctcgc cctacgcaca gccaggtcc 180
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cacagtttcg acgtgtcctt ccagcagtcg agcaccgcca agtcggccac ctggacgtat 300
tccactgaac tgaagaaact ctactgccaa attgcaaaga catgccccat ccagatcaag 360
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gagcacgtca cggaggtggt gaagcgggtg cccaaccatg agctgagccg tgaattcaac 480
gagggacaga ttgcccctcc tagtcatttg attcgagtag aggggaacag ccatgcccag 540
tatgtagaag atcccatcac aggaagacag agtgtgctgg taccttatga gccaccccag 600
gttggcactg aattcacgac agtcttgtag aatttcattg gtaacagcag ttgtgttgga 660
gggatgaacc gccgtccaat tttaatcatt gttactctgg aaaccagaga tgggcaagtc 720
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tcccagatg atgaactggt atacttacca gtgagggggt gtgagactta tgaaatgctg 960
ttgaagatca aagagtccct ggaactcatg cagtaccttc ctcagcacac aattgaaacg 1020
tacaggcaac agcaacagca gcagcaccag cacttacttc agaaacatct cctttcagcc 1080
tgcttcagga atgagcttgt ggagccccgg agagaaactc caaaacaatc tgacgtcttc 1140
ttagacatt ccaagcccc aaaccgatca gtgtaccat ag 1182

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&lt;210&gt; 306

&lt;211&gt; 586

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 306

Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln  
 1 5 10 15  
 Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn  
 20 25 30

257/299

Gly	Ser	Ser	Ser	Thr	Ser	Pro	Tyr	Asn	Thr	Asp	His	Ala	Gln	Asn	Ser	35	40	45
Val	Thr	Ala	Pro	Ser	Pro	Tyr	Ala	Gln	Pro	Ser	Ser	Thr	Phe	Asp	Ala	50	55	60
Leu	Ser	Pro	Ser	Pro	Ala	Ile	Pro	Ser	Asn	Thr	Asp	Tyr	Pro	Gly	Pro	65	70	75
His	Ser	Phe	Asp	Val	Ser	Phe	Gln	Gln	Ser	Ser	Thr	Ala	Lys	Ser	Ala	85	90	95
Thr	Trp	Thr	Tyr	Ser	Thr	Glu	Leu	Lys	Lys	Leu	Tyr	Cys	Gln	Ile	Ala	100	105	110
Lys	Thr	Cys	Pro	Ile	Gln	Ile	Lys	Val	Met	Thr	Pro	Pro	Pro	Gln	Gly	115	120	125
Ala	Val	Ile	Arg	Ala	Met	Pro	Val	Tyr	Lys	Lys	Ala	Glu	His	Val	Thr	130	135	140
Glu	Val	Val	Lys	Arg	Cys	Pro	Asn	His	Glu	Leu	Ser	Arg	Glu	Phe	Asn	145	150	155
Glu	Gly	Gln	Ile	Ala	Pro	Pro	Ser	His	Leu	Ile	Arg	Val	Glu	Gly	Asn	165	170	175
Ser	His	Ala	Gln	Tyr	Val	Glu	Asp	Pro	Ile	Thr	Gly	Arg	Gln	Ser	Val	180	185	190
Leu	Val	Pro	Tyr	Glu	Pro	Pro	Gln	Val	Gly	Thr	Glu	Phe	Thr	Thr	Val	195	200	205
Leu	Tyr	Asn	Phe	Met	Cys	Asn	Ser	Ser	Cys	Val	Gly	Gly	Met	Asn	Arg	210	215	220
Arg	Pro	Ile	Leu	Ile	Ile	Val	Thr	Leu	Glu	Thr	Arg	Asp	Gly	Gln	Val	225	230	235
Leu	Gly	Arg	Arg	Cys	Phe	Glu	Ala	Arg	Ile	Cys	Ala	Cys	Pro	Gly	Arg	245	250	255
Asp	Arg	Lys	Ala	Asp	Glu	Asp	Ser	Ile	Arg	Lys	Gln	Gln	Val	Ser	Asp	260	265	270
Ser	Thr	Lys	Asn	Gly	Asp	Gly	Thr	Lys	Arg	Pro	Phe	Arg	Gln	Asn	Thr	275	280	285
His	Gly	Ile	Gln	Met	Thr	Ser	Ile	Lys	Lys	Arg	Arg	Ser	Pro	Asp	Asp	290	295	300
Glu	Leu	Leu	Tyr	Leu	Pro	Val	Arg	Gly	Arg	Glu	Thr	Tyr	Glu	Met	Leu	305	310	315
Leu	Lys	Ile	Lys	Glu	Ser	Leu	Glu	Leu	Met	Gln	Tyr	Leu	Pro	Gln	His	325	330	335



258/299

Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln Gln His Gln His Leu  
 340 345 350  
 Leu Gln Lys Gln Thr Ser Ile Gln Ser Pro Ser Ser Tyr Gly Asn Ser  
 355 360 365  
 Ser Pro Pro Leu Asn Lys Met Asn Ser Met Asn Lys Leu Pro Ser Val  
 370 375 380  
 Ser Gln Leu Ile Asn Pro Gln Gln Arg Asn Ala Leu Thr Pro Thr Thr  
 385 390 395 400  
 Ile Pro Asp Gly Met Gly Ala Asn Ile Pro Met Met Gly Thr His Met  
 405 410 415  
 Pro Met Ala Gly Asp Met Asn Gly Leu Ser Pro Thr Gln Ala Leu Pro  
 420 425 430  
 Pro Pro Leu Ser Met Pro Ser Thr Ser His Cys Thr Pro Pro Pro Pro  
 435 440 445  
 Tyr Pro Thr Asp Cys Ser Ile Val Ser Phe Leu Ala Arg Leu Gly Cys  
 450 455 460  
 Ser Ser Cys Leu Asp Tyr Phe Thr Thr Gln Gly Leu Thr Thr Ile Tyr  
 465 470 475 480  
 Gln Ile Glu His Tyr Ser Met Asp Asp Leu Ala Ser Leu Lys Ile Pro  
 485 490 495  
 Glu Gln Phe Arg His Ala Ile Trp Lys Gly Ile Leu Asp His Arg Gln  
 500 505 510  
 Leu His Glu Phe Ser Ser Pro Ser His Leu Leu Arg Thr Pro Ser Ser  
 515 520 525  
 Ala Ser Thr Val Ser Val Gly Ser Ser Glu Thr Arg Gly Glu Arg Val  
 530 535 540  
 Ile Asp Ala Val Arg Phe Thr Leu Arg Gln Thr Ile Ser Phe Pro Pro  
 545 550 555 560  
 Arg Asp Glu Trp Asn Asp Phe Asn Phe Asp Met Asp Ala Arg Arg Asn  
 565 570 575  
 Lys Gln Gln Arg Ile Lys Glu Glu Gly Glu  
 580 585

&lt;210&gt; 307

&lt;211&gt; 1761

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 307

atgttgtagc tggaaaacaa tgcccagact caatttagtg agccacagta cacgaacctg 60  
 gggctcctga acagcatgga ccagcagatt cagaacggct cctcgtccac cagtccttat 120  
 aacacagacc acgcgcagaa cagcgtcacg gcgcctcgc cctacgcaca gccagctcc 180

259/299

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accttcgatg ctctctctcc atcacccgcc atcccctcca acaccgacta cccaggcccg 240
cacagtttcg acgtgtcctt ccagcagtcg agcacccgcc agtcggccac ctggacgtat 300
tccactgaac tgaagaaact ctactgccaa attgcaaaga catgccccat ccagatcaag 360
gtgatgaccc cacctcctca gggagctgtt atccgcgcca tgccctgtcta caaaaaagct 420
gagcacgtca cggagggtgg gaagcgggtg cccaaccatg agctgagccg tgaattcaac 480
gagggacaga ttgcccctcc tagtcatttg attcgagtag aggggaacag ccatgcccag 540
tatgtagaag atcccatcac aggaagacag agtgtgtctg taccttatga gccaccccag 600
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gggatgaacc gccgtccaat tttaatcatt gttactctgg aaaccagaga tgggcaagtc 720
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gatgaagata gcatcagaaa gcagcaagtt tcggacagta caaagaacgg tgatggtacg 840
aagcgcctgt ttcgtcagaa cacacatggt atccagatga catccatcaa gaaacgaaga 900
tccccagatg atgaactggt atacttacca gtgagggggc gtgagactta tgaaatgctg 960
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gggtgagcgtg ttattgatgc tgtgcgattc accctccgcc agaccatctc tttcccaccc 1680
cgagatgagt ggaatgactt caactttgac atggatgctc gccgcaataa gcaacagcgc 1740
atcaaagagg agggggagtg a 1761

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&lt;210&gt; 308

&lt;211&gt; 516

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 308

```

Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe
  1                      5                      10                      15

Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro
      20                      25                      30

Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn
      35                      40                      45

Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu
      50                      55                      60

Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser
      65                      70                      75                      80

Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn
      85                      90                      95

Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln
      100                      105                      110

Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser
      115                      120                      125

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260/299

Asn	Thr	Asp	Tyr	Pro	Gly	Pro	His	Ser	Phe	Asp	Val	Ser	Phe	Gln	Gln	130	135	140
Ser	Ser	Thr	Ala	Lys	Ser	Ala	Thr	Trp	Thr	Tyr	Ser	Thr	Glu	Leu	Lys	145	150	155
Lys	Leu	Tyr	Cys	Gln	Ile	Ala	Lys	Thr	Cys	Pro	Ile	Gln	Ile	Lys	Val	165	170	175
Met	Thr	Pro	Pro	Pro	Gln	Gly	Ala	Val	Ile	Arg	Ala	Met	Pro	Val	Tyr	180	185	190
Lys	Lys	Ala	Glu	His	Val	Thr	Glu	Val	Val	Lys	Arg	Cys	Pro	Asn	His	195	200	205
Glu	Leu	Ser	Arg	Glu	Phe	Asn	Glu	Gly	Gln	Ile	Ala	Pro	Pro	Ser	His	210	215	220
Leu	Ile	Arg	Val	Glu	Gly	Asn	Ser	His	Ala	Gln	Tyr	Val	Glu	Asp	Pro	225	230	235
Ile	Thr	Gly	Arg	Gln	Ser	Val	Leu	Val	Pro	Tyr	Glu	Pro	Pro	Gln	Val	245	250	255
Gly	Thr	Glu	Phe	Thr	Thr	Val	Leu	Tyr	Asn	Phe	Met	Cys	Asn	Ser	Ser	260	265	270
Cys	Val	Gly	Gly	Met	Asn	Arg	Arg	Pro	Ile	Leu	Ile	Ile	Val	Thr	Leu	275	280	285
Glu	Thr	Arg	Asp	Gly	Gln	Val	Leu	Gly	Arg	Arg	Cys	Phe	Glu	Ala	Arg	290	295	300
Ile	Cys	Ala	Cys	Pro	Gly	Arg	Asp	Arg	Lys	Ala	Asp	Glu	Asp	Ser	Ile	305	310	315
Arg	Lys	Gln	Gln	Val	Ser	Asp	Ser	Thr	Lys	Asn	Gly	Asp	Gly	Thr	Lys	325	330	335
Arg	Pro	Phe	Arg	Gln	Asn	Thr	His	Gly	Ile	Gln	Met	Thr	Ser	Ile	Lys	340	345	350
Lys	Arg	Arg	Ser	Pro	Asp	Asp	Glu	Leu	Leu	Tyr	Leu	Pro	Val	Arg	Gly	355	360	365
Arg	Glu	Thr	Tyr	Glu	Met	Leu	Leu	Lys	Ile	Lys	Glu	Ser	Leu	Glu	Leu	370	375	380
Met	Gln	Tyr	Leu	Pro	Gln	His	Thr	Ile	Glu	Thr	Tyr	Arg	Gln	Gln	Gln	385	390	395
Gln	Gln	Gln	His	Gln	His	Leu	Leu	Gln	Lys	Gln	Thr	Ser	Ile	Gln	Ser	405	410	415
Pro	Ser	Ser	Tyr	Gly	Asn	Ser	Ser	Pro	Pro	Leu	Asn	Lys	Met	Asn	Ser	420	425	430

261/299

Met Asn Lys Leu Pro Ser Val Ser Gln Leu Ile Asn Pro Gln Gln Arg  
 435 440 445

Asn Ala Leu Thr Pro Thr Thr Ile Pro Asp Gly Met Gly Ala Asn Ile  
 450 455 460

Pro Met Met Gly Thr His Met Pro Met Ala Gly Asp Met Asn Gly Leu  
 465 470 475 480

Ser Pro Thr Gln Ala Leu Pro Pro Pro Leu Ser Met Pro Ser Thr Ser  
 485 490 495

His Cys Thr Pro Pro Pro Pro Tyr Pro Thr Asp Cys Ser Ile Val Arg  
 500 505 510

Ile Trp Gln Val  
 515

&lt;210&gt; 309

&lt;211&gt; 1551

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 309

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atgtcccaga gcacacagac aaatgaattc ctcagtccag aggtttttcca gcatatctgg 60
gattttcttg aacagcctat atgttcagtt cagcccattg acttgaactt tgtggatgaa 120
ccatcagaag atggtgcgac aaacaagatt gagattagca tggactgtat ccgcatgcag 180
gactcggacc tgagtgaccc catgtggcca cagtacacga acctggggct cctgaacagc 240
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cagaacagcg tcacggcgcc ctgcacctac gcacagccca gctccacett cgatgctctc 360
tctccatcac ccgccatccc ctccaacacc gactaccag gcccgcacag tttcgacgtg 420
tccttcacgc agtcgagcac cgccaagtgc gccacctgga cgtattccac tgaactgaag 480
aaactctact gccaaattgc aaagacatgc cccatccaga tcaaggtgat gacccacact 540
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gtgggtgaagc ggtgccccaa ccatgagctg agccgtgaat tcaacgaggg acagattgcc 660
cctcctagtc atttgattcg agtagagggg aacagccatg cccagtatgt agaagatccc 720
atcacaggaa gacagagtgt gctggtacct tatgagccac cccaggttgg cactgaattc 780
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cagcagcagc accagcactt acttcagaaa cagacctcaa tacagtctcc atcttcatat 1260
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ccacctccgt atcccacaga ttgcagcatt gtcaggatct ggcaagtctg a 1551

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&lt;210&gt; 310

&lt;211&gt; 641

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

262/299

&lt;400&gt; 310

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Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe
 1              5              10              15

Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro
      20              25              30

Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn
      35              40              45

Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu
      50              55              60

Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser
      65              70              75              80

Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn
      85              90              95

Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln
      100              105              110

Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser
      115              120              125

Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln
      130              135              140

Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys
      145              150              155              160

Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val
      165              170              175

Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr
      180              185              190

Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His
      195              200              205

Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His
      210              215              220

Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro
      225              230              235              240

Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val
      245              250              255

Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser
      260              265              270

Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu
      275              280              285

Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg
      290              295              300

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263/299

Ile	Cys	Ala	Cys	Pro	Gly	Arg	Asp	Arg	Lys	Ala	Asp	Glu	Asp	Ser	Ile	305	310	315	320
Arg	Lys	Gln	Gln	Val	Ser	Asp	Ser	Thr	Lys	Asn	Gly	Asp	Gly	Thr	Lys	325	330	335	
Arg	Pro	Phe	Arg	Gln	Asn	Thr	His	Gly	Ile	Gln	Met	Thr	Ser	Ile	Lys	340	345	350	
Lys	Arg	Arg	Ser	Pro	Asp	Asp	Glu	Leu	Leu	Tyr	Leu	Pro	Val	Arg	Gly	355	360	365	
Arg	Glu	Thr	Tyr	Glu	Met	Leu	Leu	Lys	Ile	Lys	Glu	Ser	Leu	Glu	Leu	370	375	380	
Met	Gln	Tyr	Leu	Pro	Gln	His	Thr	Ile	Glu	Thr	Tyr	Arg	Gln	Gln	Gln	385	390	395	400
Gln	Gln	Gln	His	Gln	His	Leu	Leu	Gln	Lys	Gln	Thr	Ser	Ile	Gln	Ser	405	410	415	
Pro	Ser	Ser	Tyr	Gly	Asn	Ser	Ser	Pro	Pro	Leu	Asn	Lys	Met	Asn	Ser	420	425	430	
Met	Asn	Lys	Leu	Pro	Ser	Val	Ser	Gln	Leu	Ile	Asn	Pro	Gln	Gln	Arg	435	440	445	
Asn	Ala	Leu	Thr	Pro	Thr	Thr	Ile	Pro	Asp	Gly	Met	Gly	Ala	Asn	Ile	450	455	460	
Pro	Met	Met	Gly	Thr	His	Met	Pro	Met	Ala	Gly	Asp	Met	Asn	Gly	Leu	465	470	475	480
Ser	Pro	Thr	Gln	Ala	Leu	Pro	Pro	Pro	Leu	Ser	Met	Pro	Ser	Thr	Ser	485	490	495	
His	Cys	Thr	Pro	Pro	Pro	Tyr	Pro	Thr	Asp	Cys	Ser	Ile	Val	Ser		500	505	510	
Phe	Leu	Ala	Arg	Leu	Gly	Cys	Ser	Ser	Cys	Leu	Asp	Tyr	Phe	Thr	Thr	515	520	525	
Gln	Gly	Leu	Thr	Thr	Ile	Tyr	Gln	Ile	Glu	His	Tyr	Ser	Met	Asp	Asp	530	535	540	
Leu	Ala	Ser	Leu	Lys	Ile	Pro	Glu	Gln	Phe	Arg	His	Ala	Ile	Trp	Lys	545	550	555	560
Gly	Ile	Leu	Asp	His	Arg	Gln	Leu	His	Glu	Phe	Ser	Ser	Pro	Ser	His	565	570	575	
Leu	Leu	Arg	Thr	Pro	Ser	Ser	Ala	Ser	Thr	Val	Ser	Val	Gly	Ser	Ser	580	585	590	
Glu	Thr	Arg	Gly	Glu	Arg	Val	Ile	Asp	Ala	Val	Arg	Phe	Thr	Leu	Arg	595	600	605	
Gln	Thr	Ile	Ser	Phe	Pro	Pro	Arg	Asp	Glu	Trp	Asn	Asp	Phe	Asn	Phe				

264/299

610 615 620

Asp Met Asp Ala Arg Arg Asn Lys Gln Gln Arg Ile Lys Glu Glu Gly  
625 630 635 640

Glu

<210> 311  
<211> 1926  
<212> DNA  
<213> Homo sapiens

<400> 311  
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<210> 312  
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<212> PRT  
<213> Homo sapiens

<400> 312  
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265/299

Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro  
 20 25 30  
 Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn  
 35 40 45  
 Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu  
 50 55 60  
 Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser  
 65 70 75 80  
 Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn  
 85 90 95  
 Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln  
 100 105 110  
 Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser  
 115 120 125  
 Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln  
 130 135 140  
 Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys  
 145 150 155 160  
 Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val  
 165 170 175  
 Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr  
 180 185 190  
 Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His  
 195 200 205  
 Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His  
 210 215 220  
 Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro  
 225 230 235 240  
 Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val  
 245 250 255  
 Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser  
 260 265 270  
 Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu  
 275 280 285  
 Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg  
 290 295 300  
 Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile  
 305 310 315 320  
 Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys



266/299

325	330	335
Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys		
340	345	350
Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly		
355	360	365
Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu		
370	375	380
Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln		
385	390	395
Gln Gln Gln His Gln His Leu Leu Gln Lys His Leu Leu Ser Ala Cys		
405	410	415
Phe Arg Asn Glu Leu Val Glu Pro Arg Arg Glu Thr Pro Lys Gln Ser		
420	425	430
Asp Val Phe Phe Arg His Ser Lys Pro Pro Asn Arg Ser Val Tyr Pro		
435	440	445

&lt;210&gt; 313

&lt;211&gt; 2816

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 313

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267/299

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&lt;210&gt; 314

&lt;211&gt; 499

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 314

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Met Ala Gln Ser Thr Ala Thr Ser Pro Asp Gly Gly Thr Thr Phe Glu
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His Leu Trp Ser Ser Leu Glu Pro Asp Ser Thr Tyr Phe Asp Leu Pro
      20              25              30

Gln Ser Ser Arg Gly Asn Asn Glu Val Val Gly Gly Thr Asp Ser Ser
      35              40              45

Met Asp Val Phe His Leu Glu Gly Met Thr Thr Ser Val Met Ala Gln
      50              55              60

Phe Asn Leu Leu Ser Ser Thr Met Asp Gln Met Ser Ser Arg Ala Ala
      65              70              75              80

Ser Ala Ser Pro Tyr Thr Pro Glu His Ala Ala Ser Val Pro Thr His
      85              90              95

Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Thr Met Ser Pro Ala
      100              105              110

Pro Val Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro His His Phe Glu
      115              120              125

Val Thr Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr
      130              135              140

Ser Pro Leu Leu Lys Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro
      145              150              155              160

Ile Gln Ile Lys Val Ser Thr Pro Pro Pro Pro Gly Thr Ala Ile Arg

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268/299

165					170					175					
Ala	Met	Pro	Val	Tyr	Lys	Lys	Ala	Glu	His	Val	Thr	Asp	Val	Val	Lys
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Arg	Cys	Pro	Asn	His	Glu	Leu	Gly	Arg	Asp	Phe	Asn	Glu	Gly	Gln	Ser
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Ala	Pro	Ala	Ser	His	Leu	Ile	Arg	Val	Glu	Gly	Asn	Asn	Leu	Ser	Gln
		210				215					220				
Tyr	Val	Asp	Asp	Pro	Val	Thr	Gly	Arg	Gln	Ser	Val	Val	Val	Pro	Tyr
225					230					235					240
Glu	Pro	Pro	Gln	Val	Gly	Thr	Glu	Phe	Thr	Thr	Ile	Leu	Tyr	Asn	Phe
			245						250					255	
Met	Cys	Asn	Ser	Ser	Cys	Val	Gly	Gly	Met	Asn	Arg	Arg	Pro	Ile	Leu
			260					265					270		
Ile	Ile	Ile	Thr	Leu	Glu	Met	Arg	Asp	Gly	Gln	Val	Leu	Gly	Arg	Arg
		275					280					285			
Ser	Phe	Glu	Gly	Arg	Ile	Cys	Ala	Cys	Pro	Gly	Arg	Asp	Arg	Lys	Ala
	290					295					300				
Asp	Glu	Asp	His	Tyr	Arg	Glu	Gln	Gln	Ala	Leu	Asn	Glu	Ser	Ser	Ala
305					310					315					320
Lys	Asn	Gly	Ala	Ala	Ser	Lys	Arg	Ala	Phe	Lys	Gln	Ser	Pro	Pro	Ala
			325						330					335	
Val	Pro	Ala	Leu	Gly	Ala	Gly	Val	Lys	Lys	Arg	Arg	His	Gly	Asp	Glu
			340					345					350		
Asp	Thr	Tyr	Tyr	Leu	Gln	Val	Arg	Gly	Arg	Glu	Asn	Phe	Glu	Ile	Leu
		355					360					365			
Met	Lys	Leu	Lys	Glu	Ser	Leu	Glu	Leu	Met	Glu	Leu	Val	Pro	Gln	Pro
		370				375					380				
Leu	Val	Asp	Ser	Tyr	Arg	Gln	Gln	Gln	Gln	Leu	Leu	Gln	Arg	Pro	Ser
385					390					395					400
His	Leu	Gln	Pro	Pro	Ser	Tyr	Gly	Pro	Val	Leu	Ser	Pro	Met	Asn	Lys
			405						410					415	
Val	His	Gly	Gly	Met	Asn	Lys	Leu	Pro	Ser	Val	Asn	Gln	Leu	Val	Gly
			420					425					430		
Gln	Pro	Pro	Pro	His	Ser	Ser	Ala	Ala	Thr	Pro	Asn	Leu	Gly	Pro	Val
		435					440					445			
Gly	Pro	Gly	Met	Leu	Asn	Asn	His	Gly	His	Ala	Val	Pro	Ala	Asn	Gly
		450				455					460				
Glu	Met	Ser	Ser	Ser	His	Ser	Ala	Gln	Ser	Met	Val	Ser	Gly	Ser	His
465					470					475					480

269/299

Cys Thr Pro Pro Pro Pro Tyr His Ala Asp Pro Ser Leu Val Arg Thr  
                   485                  490                  495

Trp Gly Pro

<210> 315

<211> 636

<212> PRT

<213> Homo sapiens

<400> 315

Met Ala Gln Ser Thr Ala Thr Ser Pro Asp Gly Gly Thr Thr Phe Glu  
   1                  5                  10                  15

His Leu Trp Ser Ser Leu Glu Pro Asp Ser Thr Tyr Phe Asp Leu Pro  
                   20                  25                  30

Gln Ser Ser Arg Gly Asn Asn Glu Val Val Gly Gly Thr Asp Ser Ser  
                   35                  40                  45

Met Asp Val Phe His Leu Glu Gly Met Thr Thr Ser Val Met Ala Gln  
   50                  55                  60

Phe Asn Leu Leu Ser Ser Thr Met Asp Gln Met Ser Ser Arg Ala Ala  
   65                  70                  75                  80

Ser Ala Ser Pro Tyr Thr Pro Glu His Ala Ala Ser Val Pro Thr His  
                   85                  90                  95

Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Thr Met Ser Pro Ala  
                   100                  105                  110

Pro Val Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro His His Phe Glu  
                   115                  120                  125

Val Thr Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr  
   130                  135                  140

Ser Pro Leu Leu Lys Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro  
   145                  150                  155                  160

Ile Gln Ile Lys Val Ser Thr Pro Pro Pro Gly Thr Ala Ile Arg  
                   165                  170                  175

Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr Asp Val Val Lys  
                   180                  185                  190

Arg Cys Pro Asn His Glu Leu Gly Arg Asp Phe Asn Glu Gly Gln Ser  
                   195                  200                  205

Ala Pro Ala Ser His Leu Ile Arg Val Glu Gly Asn Asn Leu Ser Gln  
   210                  215                  220

Tyr Val Asp Asp Pro Val Thr Gly Arg Gln Ser Val Val Val Pro Tyr  
   225                  230                  235                  240

270/299

Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Ile Leu Tyr Asn Phe  
 245 250 255  
 Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu  
 260 265 270  
 Ile Ile Ile Thr Leu Glu Met Arg Asp Gly Gln Val Leu Gly Arg Arg  
 275 280 285  
 Ser Phe Glu Gly Arg Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala  
 290 295 300  
 Asp Glu Asp His Tyr Arg Glu Gln Gln Ala Leu Asn Glu Ser Ser Ala  
 305 310 315 320  
 Lys Asn Gly Ala Ala Ser Lys Arg Ala Phe Lys Gln Ser Pro Pro Ala  
 325 330 335  
 Val Pro Ala Leu Gly Ala Gly Val Lys Lys Arg Arg His Gly Asp Glu  
 340 345 350  
 Asp Thr Tyr Tyr Leu Gln Val Arg Gly Arg Glu Asn Phe Glu Ile Leu  
 355 360 365  
 Met Lys Leu Lys Glu Ser Leu Glu Leu Met Glu Leu Val Pro Gln Pro  
 370 375 380  
 Leu Val Asp Ser Tyr Arg Gln Gln Gln Gln Leu Leu Gln Arg Pro Ser  
 385 390 395 400  
 His Leu Gln Pro Pro Ser Tyr Gly Pro Val Leu Ser Pro Met Asn Lys  
 405 410 415  
 Val His Gly Gly Met Asn Lys Leu Pro Ser Val Asn Gln Leu Val Gly  
 420 425 430  
 Gln Pro Pro Pro His Ser Ser Ala Ala Thr Pro Asn Leu Gly Pro Val  
 435 440 445  
 Gly Pro Gly Met Leu Asn Asn His Gly His Ala Val Pro Ala Asn Gly  
 450 455 460  
 Glu Met Ser Ser Ser His Ser Ala Gln Ser Met Val Ser Gly Ser His  
 465 470 475 480  
 Cys Thr Pro Pro Pro Pro Tyr His Ala Asp Pro Ser Leu Val Ser Phe  
 485 490 495  
 Leu Thr Gly Leu Gly Cys Pro Asn Cys Ile Glu Tyr Phe Thr Ser Gln  
 500 505 510  
 Gly Leu Gln Ser Ile Tyr His Leu Gln Asn Leu Thr Ile Glu Asp Leu  
 515 520 525  
 Gly Ala Leu Lys Ile Pro Glu Gln Tyr Arg Met Thr Ile Trp Arg Gly  
 530 535 540  
 Leu Gln Asp Leu Lys Gln Gly His Asp Tyr Ser Thr Ala Gln Gln Leu

545	550							555							560	
Leu	Arg	Ser	Ser	Asn	Ala	Ala	Thr	Ile	Ser	Ile	Gly	Gly	Ser	Gly	Glu	
				565					570					575		
Leu	Gln	Arg	Gln	Arg	Val	Met	Glu	Ala	Val	His	Phe	Arg	Val	Arg	His	
				580					585					590		
Thr	Ile	Thr	Ile	Pro	Asn	Arg	Gly	Gly	Pro	Gly	Gly	Gly	Pro	Asp	Glu	
				595					600					605		
Trp	Ala	Asp	Phe	Gly	Phe	Asp	Leu	Pro	Asp	Cys	Lys	Ala	Arg	Lys	Gln	
				610					615					620		
Pro	Ile	Lys	Glu	Glu	Phe	Thr	Glu	Ala	Glu	Ile	His					
				625					630					635		

<400> 316															
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Phe	Asn	Leu	Leu	Ser	Ser	Thr	Met	Asp	Gln	Met	Ser	Ser	Arg	Ala	Ala
			20					25					30		
Ser	Ala	Ser	Pro	Tyr	Thr	Pro	Glu	His	Ala	Ala	Ser	Val	Pro	Thr	His
		35					40					45			
Ser	Pro	Tyr	Ala	Gln	Pro	Ser	Ser	Thr	Phe	Asp	Thr	Met	Ser	Pro	Ala
	50					55					60				
Pro	Val	Ile	Pro	Ser	Asn	Thr	Asp	Tyr	Pro	Gly	Pro	His	His	Phe	Glu
65					70					75					80
Val	Thr	Phe	Gln	Gln	Ser	Ser	Thr	Ala	Lys	Ser	Ala	Thr	Trp	Thr	Tyr
				85					90					95	
Ser	Pro	Leu	Leu	Lys	Lys	Leu	Tyr	Cys	Gln	Ile	Ala	Lys	Thr	Cys	Pro
		100						105					110		
Ile	Gln	Ile	Lys	Val	Ser	Thr	Pro	Pro	Pro	Pro	Gly	Thr	Ala	Ile	Arg
		115					120					125			
Ala	Met	Pro	Val	Tyr	Lys	Lys	Ala	Glu	His	Val	Thr	Asp	Val	Val	Lys
	130					135					140				
Arg	Cys	Pro	Asn	His	Glu	Leu	Gly	Arg	Asp	Phe	Asn	Glu	Gly	Gln	Ser
145				150						155					160
Ala	Pro	Ala	Ser	His	Leu	Ile	Arg	Val	Glu	Gly	Asn	Asn	Leu	Ser	Gln
				165					170					175	
Tyr	Val	Asp	Asp	Pro	Val	Thr	Gly	Arg	Gln	Ser	Val	Val	Val	Pro	Tyr

272/299

180					185					190					
Glu	Pro	Pro	Gln	Val	Gly	Thr	Glu	Phe	Thr	Thr	Ile	Leu	Tyr	Asn	Phe
		195					200					205			
Met	Cys	Asn	Ser	Ser	Cys	Val	Gly	Gly	Met	Asn	Arg	Arg	Pro	Ile	Leu
	210					215					220				
Ile	Ile	Ile	Thr	Leu	Glu	Met	Arg	Asp	Gly	Gln	Val	Leu	Gly	Arg	Arg
225						230					235				240
Ser	Phe	Glu	Gly	Arg	Ile	Cys	Ala	Cys	Pro	Gly	Arg	Asp	Arg	Lys	Ala
				245					250					255	
Asp	Glu	Asp	His	Tyr	Arg	Glu	Gln	Gln	Ala	Leu	Asn	Glu	Ser	Ser	Ala
			260					265					270		
Lys	Asn	Gly	Ala	Ala	Ser	Lys	Arg	Ala	Phe	Lys	Gln	Ser	Pro	Pro	Ala
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Val	Pro	Ala	Leu	Gly	Ala	Gly	Val	Lys	Lys	Arg	Arg	His	Gly	Asp	Glu
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305						310					315				320
Met	Lys	Leu	Lys	Glu	Ser	Leu	Glu	Leu	Met	Glu	Leu	Val	Pro	Gln	Pro
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Leu	Val	Asp	Ser	Tyr	Arg	Gln	Gln	Gln	Gln	Leu	Leu	Gln	Arg	Pro	Ser
			340				345						350		
His	Leu	Gln	Pro	Pro	Ser	Tyr	Gly	Pro	Val	Leu	Ser	Pro	Met	Asn	Lys
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Val	His	Gly	Gly	Met	Asn	Lys	Leu	Pro	Ser	Val	Asn	Gln	Leu	Val	Gly
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Gln	Pro	Pro	Pro	His	Ser	Ser	Ala	Ala	Thr	Pro	Asn	Leu	Gly	Pro	Val
385						390					395				400
Gly	Pro	Gly	Met	Leu	Asn	Asn	His	Gly	His	Ala	Val	Pro	Ala	Asn	Gly
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Glu	Met	Ser	Ser	Ser	His	Ser	Ala	Gln	Ser	Met	Val	Ser	Gly	Ser	His
			420					425					430		
Cys	Thr	Pro	Pro	Pro	Pro	Tyr	His	Ala	Asp	Pro	Ser	Leu	Val	Ser	Phe
		435					440					445			
Leu	Thr	Gly	Leu	Gly	Cys	Pro	Asn	Cys	Ile	Glu	Tyr	Phe	Thr	Ser	Gln
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Gly	Leu	Gln	Ser	Ile	Tyr	His	Leu	Gln	Asn	Leu	Thr	Ile	Glu	Asp	Leu
465						470					475				480
Gly	Ala	Leu	Lys	Ile	Pro	Glu	Gln	Tyr	Arg	Met	Thr	Ile	Trp	Arg	Gly
				485					490					495	

273/299

Leu Gln Asp Leu Lys Gln Gly His Asp Tyr Ser Thr Ala Gln Gln Leu  
 500 505 510  
 Leu Arg Ser Ser Asn Ala Ala Thr Ile Ser Ile Gly Gly Ser Gly Glu  
 515 520 525  
 Leu Gln Arg Gln Arg Val Met Glu Ala Val His Phe Arg Val Arg His  
 530 535 540  
 Thr Ile Thr Ile Pro Asn Arg Gly Gly Pro Gly Gly Gly Pro Asp Glu  
 545 550 555 560  
 Trp Ala Asp Phe Gly Phe Asp Leu Pro Asp Cys Lys Ala Arg Lys Gln  
 565 570 575  
 Pro Ile Lys Glu Glu Phe Thr Glu Ala Glu Ile His  
 580 585

&lt;210&gt; 317

&lt;211&gt; 2234

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 317

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aggggacgca gcgaaaccgg ggcccgcgcc aggccagccg ggacggacgc cgatgcccgg 60
ggctgcgacg gctgcagagc gagctgccct cggaggccgg cgtggggaag atggcccagt 120
ccaccgccac ctcccctgat gggggcacca cgtttgagca cctctggagc tctctggaac 180
cagacagcac ctacttcgac cttccccagt caagccgggg gaataatgag gtggtgggcg 240
gaacggattc cagcatggac gtcttccacc tggagggcag gactacatct gtcatggccc 300
agttcaatct gctgagcagc accatggacc agatgagcag ccgcgcggcc tcggccagcc 360
cctacacccc agagcacgcc gccagcgtgc ccaccactc gccctacgca caaccagct 420
ccaccttoga caccatgtcg ccggcgcctg tcatccctc caacaccgac taccgccgac 480
cccaccactt tgaggtcact ttccagcagt ccagcacggc caagtcagcc acctggacgt 540
actccccgct cttgaagaaa ctctactgcc agatcgccaa gacatgcccc atccagatca 600
aggtgtccac cccgccaccc ccaggcactg ccatccgggc catgacctgt tacaagaaag 660
cggagcacgt gaccgacgtc gtgaaacgct gccccacca cgagctcggg agggacttca 720
acgaaggaca gtctgctcca gccagccacc tcatccgctt ggaaggcaat aatctctcgc 780
agtatgtgga tgaccctgtc accggcaggc agagcgtcgt ggtgccctat gagccaccac 840
aggtggggac ggaattcacc accatcctgt acaacttcat gtgtaacagc agctgtgtag 900
ggggcatgaa ccggcggccc atcctcatca tcatcaccct ggagatgcgg gatgggcagg 960
tgctgggccc ccggtccttt gagggccgca tctgcgcctg tcctggccgc gaccgaaaag 1020
ctgatgagga ccactaccgg gagcagcagg ccctgaacga gagctccgcc aagaacgggg 1080
ccgccagcaa gcgtgccttc aagcagagcc cccctgcgct ccccgccctt ggtgccggtg 1140
tgaagaagcg gcggcatgga gacgaggaca cgtactacct tcaggtgoga ggccgggaga 1200
actttgagat cctgatgaag ctgaaagaga gcctggagct gatggagtgt gtgccgcagc 1260
cactggtgga ctccatcggc cagcagcagc agctcctaca gaggccgagt cacctacagc 1320
ccccgtccta cgggccgggtc ctctcgccca tgaacaaggt gcacgggggc atgaacaagc 1380
tgccctccgt caaccagctg gtgggcccagc ctcccccgca cagttcggca gctacacca 1440
acctggggcc cgtgggcccc gggatgtca acaaccatgg ccacgcagtg ccagccaacg 1500
gcgagatgag cagcagccac agcgcgccagt ccattggtctc ggggtcccac tgcaactccg 1560
caccacctta ccacgccgac ccagcctcg tcagtttttt aacaggattg ggggtgtccaa 1620
actgcatcga gtatttcacc tcccaagggt tacagagcat ttaccacctg cagaacctga 1680
ccattgagga cctggggggc ctgaagatcc ccgagcagta ccgcatgacc atctggcggg 1740
gcatgcagga cctgaagcag ggccacgact acagcaccgc gcagcagctg ctccgctcta 1800
gcaacgcggc caccatctcc atcggcggct caggggaact gcagcgccag cgggtcatgtg 1860
agggcgtgca cttccgcgtg cgccacacca tcaccatccc caaccgcggc ggcccaggcg 1920

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274/299

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gcgggccctga cgagtgggcg gacttcgggt tcgacctgcc cgactgcaag gcccgcaagc 1980
agcccatcaa ggaggagttc acggaggccg agatccactg agggcctcgc ctggctgcag 2040
cctgcgccac cgcccagaga cccaagctgc ctcccctctc cttcctgtgt gtccaaaact 2100
gcctcaggag gcaggacctt cgggctgtgc ccggggaaag gcaagggtccg gcccattccc 2160
aggcacctca caggccccag gaaaggccca gccaccgaag ccgcctgtgg acagcctgag 2220
tcacctgcag aacc                                     2234

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&lt;210&gt; 318

&lt;211&gt; 732

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 318

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Met Pro Glu Glu Thr Gln Thr Gln Asp Gln Pro Met Glu Glu Glu Glu
  1                      5                      10                      15

Val Glu Thr Phe Ala Phe Gln Ala Glu Ile Ala Gln Leu Met Ser Leu
                20                      25                      30

Ile Ile Asn Thr Phe Tyr Ser Asn Lys Glu Ile Phe Leu Arg Glu Leu
    35                      40                      45

Ile Ser Asn Ser Ser Asp Ala Leu Asp Lys Ile Arg Tyr Glu Thr Leu
    50                      55                      60

Thr Asp Pro Ser Lys Leu Asp Ser Gly Lys Glu Leu His Ile Asn Leu
    65                      70                      75                      80

Ile Pro Asn Lys Gln Asp Arg Thr Leu Thr Ile Val Asp Thr Gly Ile
                85                      90                      95

Gly Met Thr Lys Ala Asp Leu Ile Asn Asn Leu Gly Thr Ile Ala Lys
    100                      105                      110

Ser Gly Thr Lys Ala Phe Met Glu Ala Leu Gln Ala Gly Ala Asp Ile
    115                      120                      125

Ser Met Ile Gly Gln Phe Gly Val Gly Phe Tyr Ser Ala Tyr Leu Val
    130                      135                      140

Ala Glu Lys Val Thr Val Ile Thr Lys His Asn Asp Asp Glu Gln Tyr
    145                      150                      155                      160

Ala Trp Glu Ser Ser Ala Gly Gly Ser Phe Thr Val Arg Thr Asp Thr
                165                      170                      175

Gly Glu Pro Met Gly Arg Gly Thr Lys Val Ile Leu His Leu Lys Glu
    180                      185                      190

Asp Gln Thr Glu Tyr Leu Glu Glu Arg Arg Ile Lys Glu Ile Val Lys
    195                      200                      205

Lys His Ser Gln Phe Ile Gly Tyr Pro Ile Thr Leu Phe Val Glu Lys
    210                      215                      220

Glu Arg Asp Lys Glu Val Ser Asp Asp Glu Ala Glu Glu Lys Glu Asp
    225                      230                      235                      240

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275/299

Lys Glu Glu Glu Lys Glu Lys Glu Glu Lys Glu Ser Glu Asp Lys Pro  
 245 250 255  
 Glu Ile Glu Asp Val Gly Ser Asp Glu Glu Glu Glu Lys Lys Asp Gly  
 260 265 270  
 Asp Lys Lys Lys Lys Lys Lys Ile Lys Glu Lys Tyr Ile Asp Gln Glu  
 275 280 285  
 Glu Leu Asn Lys Thr Lys Pro Ile Trp Thr Arg Asn Pro Asp Asp Ile  
 290 295 300  
 Thr Asn Glu Glu Tyr Gly Glu Phe Tyr Lys Ser Leu Thr Asn Asp Trp  
 305 310 315 320  
 Glu Asp His Leu Ala Val Lys His Phe Ser Val Glu Gly Gln Leu Glu  
 325 330 335  
 Phe Arg Ala Leu Leu Phe Val Pro Arg Arg Ala Pro Phe Asp Leu Phe  
 340 345 350  
 Glu Asn Arg Lys Lys Lys Asn Asn Ile Lys Leu Tyr Val Arg Arg Val  
 355 360 365  
 Phe Ile Met Asp Asn Cys Glu Glu Leu Ile Pro Glu Tyr Leu Asn Phe  
 370 375 380  
 Ile Arg Gly Val Val Asp Ser Glu Asp Leu Pro Leu Asn Ile Ser Arg  
 385 390 395 400  
 Glu Met Leu Gln Gln Ser Lys Ile Leu Lys Val Ile Arg Lys Asn Leu  
 405 410 415  
 Val Lys Lys Cys Leu Glu Leu Phe Thr Glu Leu Ala Glu Asp Lys Glu  
 420 425 430  
 Asn Tyr Lys Lys Phe Tyr Glu Gln Phe Ser Lys Asn Ile Lys Leu Gly  
 435 440 445  
 Ile His Glu Asp Ser Gln Asn Arg Lys Lys Leu Ser Glu Leu Leu Arg  
 450 455 460  
 Tyr Tyr Thr Ser Ala Ser Gly Asp Glu Met Val Ser Leu Lys Asp Tyr  
 465 470 475 480  
 Cys Thr Arg Met Lys Glu Asn Gln Lys His Ile Tyr Tyr Ile Thr Gly  
 485 490 495  
 Glu Thr Lys Asp Gln Val Ala Asn Ser Ala Phe Val Glu Arg Leu Arg  
 500 505 510  
 Lys His Gly Leu Glu Val Ile Tyr Met Ile Glu Pro Ile Asp Glu Tyr  
 515 520 525  
 Cys Val Gln Gln Leu Lys Glu Phe Glu Gly Lys Thr Leu Val Ser Val  
 530 535 540

276/299

Thr Lys Glu Gly Leu Glu Leu Pro Glu Asp Glu Glu Glu Lys Lys Lys  
 545 550 555 560  
 Gln Glu Glu Lys Lys Thr Lys Phe Glu Asn Leu Cys Lys Ile Met Lys  
 565 570 575  
 Asp Ile Leu Glu Lys Lys Val Glu Lys Val Val Val Ser Asn Arg Leu  
 580 585 590  
 Val Thr Ser Pro Cys Cys Ile Val Thr Ser Thr Tyr Gly Trp Thr Ala  
 595 600 605  
 Asn Met Glu Arg Ile Met Lys Ala Gln Ala Leu Arg Asp Asn Ser Thr  
 610 615 620  
 Met Gly Tyr Met Ala Ala Lys Lys His Leu Glu Ile Asn Pro Asp His  
 625 630 635 640  
 Ser Ile Ile Glu Thr Leu Arg Gln Lys Ala Glu Ala Asp Lys Asn Asp  
 645 650 655  
 Lys Ser Val Lys Asp Leu Val Ile Leu Leu Tyr Glu Thr Ala Leu Leu  
 660 665 670  
 Ser Ser Gly Phe Ser Leu Glu Asp Pro Gln Thr His Ala Asn Arg Ile  
 675 680 685  
 Tyr Arg Met Ile Lys Leu Gly Leu Gly Ile Asp Glu Asp Asp Pro Thr  
 690 695 700  
 Ala Asp Asp Thr Ser Ala Ala Val Thr Glu Glu Met Pro Pro Leu Glu  
 705 710 715 720  
 Gly Asp Asp Asp Thr Ser Arg Met Glu Glu Val Asp  
 725 730

&lt;210&gt; 319

&lt;211&gt; 249

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 319

Met Lys Glu Thr Gln Lys Ser Thr Tyr Tyr Ile Thr Gly Glu Ser Lys  
 1 5 10 15  
 Glu Gln Val Ala Asn Ser Ala Phe Val Glu Arg Val Arg Lys Gln Gly  
 20 25 30  
 Phe Glu Val Val Tyr Met Thr Glu Pro Ile Asp Glu Tyr Cys Val Gln  
 35 40 45  
 Gln Leu Lys Glu Phe Asp Gly Lys Ser Leu Val Ser Val Thr Lys Glu  
 50 55 60  
 Gly Leu Glu Leu Pro Glu Asp Glu Glu Glu Lys Lys Lys Met Glu Glu  
 65 70 75 80

277/299

Ser Lys Glu Lys Phe Glu Asn Leu Cys Lys Leu Met Lys Glu Ile Leu  
85 90 95

Asp Lys Lys Val Glu Lys Val Thr Ile Ser Asn Arg Leu Val Ser Ser  
100 105 110

Pro Cys Cys Ile Val Thr Ser Thr Tyr Gly Trp Thr Ala Asn Met Glu  
115 120 125

Gln Ile Met Lys Ala Gln Ala Leu Arg Asp Asn Ser Thr Met Gly Tyr  
130 135 140

Met Met Ala Lys Lys His Leu Glu Ile Asn Pro Asp His Pro Ile Met  
145 150 155 160

Glu Thr Leu Arg Gln Lys Ala Glu Ala Asp Lys Asn Asp Lys Ala Val  
165 170 175

Lys Asp Leu Val Val Leu Leu Phe Glu Thr Ala Leu Leu Ser Ser Gly  
180 185 190

Phe Ser Leu Glu Asp Pro Gln Thr His Ser Asn His Ile Tyr His Met  
195 200 205

Ile Lys Leu Gly Leu Gly Thr Asp Glu Asp Glu Val Ala Ala Glu Glu  
210 215 220

Pro Ser Asp Ala Val Pro Asp Glu Ile Pro Pro Leu Glu Gly Asp Glu  
225 230 235 240

Asp Ala Ser Arg Met Glu Glu Val Asp  
245

&lt;210&gt; 320

&lt;211&gt; 1313

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 320

tggtgtggtt gactctgagg atctgcccct gaacatctgc cgagagatgc tccagcagag 60  
caaaatcttg aaagtcattc gcaaaaacat tgtaagaag tgccttgagc tcttctctga 120  
gctggcagaa gacaaggaga ttataagaaa ttctatgagg cattttctaa aaatctcaag 180  
cttggaatcc acgaagactc cactaaccgc caccgcctgt ctgagctgct gcgctgtcac 240  
acctcccagt ctggagatga gatgacatct ctgtcgtagt atgtttctca catgaaggag 300  
acacagaagt ccacctatta catcactggt gagagcaaag agcagggtggc caactctgct 360  
tttgtggagc gagtgcggaa acagggcttc gaggtggtat atatgactga gccattgac 420  
gagtactgtg tgcagcagct caaggagttt gatgggaaaa gcctggtctc agttaccaag 480  
gaggggtctgg agctacctga ggatgaggag gagaagaaga agatggaaga aagcaaggaa 540  
aagtttgaga acctctgcaa gctcatgaaa gaaatcttag ataagaaggt tgagaagggtg 600  
acaatctcca atagacttgt gtcttcaccc tgctgcattg tgaccagcac ctacggctgg 660  
acagccaata tggagcagat catgaaagcc caggcacttc gggacaactc caccatgggc 720  
tatatgatgg ccaaaaagca cctggagatc aaccccgacc accccatcat ggagacgctg 780  
cggcagaagg ctgaggccga caagaatgat aaggcagtta aggacctggt ggtgctgctg 840  
tttgaaaccg ccctgctatc ttcgggcttt tcccttgagg atccccagac ccactccaac 900  
cacacttacc acatgatcaa gctaggtcta ggtactgatg aagatgaagt ggcagcagag 960  
gaacccagtg atgcagttcc tgatgagatc cccctcttg agggatgatg ggtgctgctc 1020  
cgcatggaag aagtcgatta ggagttcata gttggaaaac ttgtgccctt gtatagtgtc 1080

278/299

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cccatggctc ccactgcagc ctcgagtgcc cctgtccac ctggctgctg gtgtctagtg 1140
tttttttccc tctcctgtcc ttgtgttgaa ggcaggaaac caaggggtgc aagccccatt 1200
ccctctctac tcttgacagc aggattggat gttgtgtatt gtggtttatt ttattttctt 1260
cattttgttc tgaaattaaa gaatgtaaaa taaagaatat gccgttttta tac 1313

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&lt;210&gt; 321

&lt;211&gt; 724

&lt;212&gt; PRT

&lt;213&gt; Mus musculus

&lt;400&gt; 321

```

Met Pro Glu Glu Val His His Gly Glu Glu Glu Val Glu Thr Phe Ala
  1                      5                      10                      15

Phe Gln Ala Glu Ile Ala Gln Leu Met Ser Leu Ile Ile Asn Thr Phe
          20                      25                      30

Tyr Ser Asn Lys Glu Ile Phe Leu Arg Glu Leu Ile Ser Asn Ala Ser
          35                      40                      45

Asp Ala Leu Asp Lys Ile Arg Tyr Glu Ser Leu Thr Asp Pro Ser Lys
  50                      55                      60

Leu Asp Ser Gly Lys Glu Leu Lys Ile Asp Ile Leu Pro Asn Pro Gln
  65                      70                      75                      80

Glu Arg Thr Leu Thr Leu Val Asp Thr Gly Ile Gly Met Thr Lys Ala
          85                      90                      95

Asp Leu Ile Asn Asn Leu Gly Thr Ile Ala Lys Ser Gly Thr Lys Ala
          100                      105                      110

Phe Met Glu Ala Leu Gln Ala Gly Ala Asp Ile Ser Met Ile Gly Gln
          115                      120                      125

Phe Gly Val Gly Phe Tyr Ser Ala Tyr Leu Val Ala Glu Lys Val Val
          130                      135                      140

Val Ile Thr Lys His Asn Asp Asp Glu Gln Tyr Ala Trp Glu Ser Ser
          145                      150                      155                      160

Ala Gly Gly Ser Phe Thr Val Arg Ala Asp His Gly Glu Pro Ile Gly
          165                      170                      175

Arg Gly Thr Lys Val Ile Leu His Leu Lys Glu Asp Gln Thr Glu Tyr
          180                      185                      190

Leu Glu Glu Arg Arg Val Lys Glu Val Val Lys Lys His Ser Gln Phe
          195                      200                      205

Ile Gly Tyr Pro Ile Thr Leu Tyr Leu Glu Lys Glu Arg Glu Lys Glu
          210                      215                      220

Ile Ser Asp Asp Glu Ala Glu Glu Glu Lys Gly Glu Lys Glu Glu Glu
          225                      230                      235                      240

Asp Lys Glu Asp Glu Glu Lys Pro Lys Ile Glu Asp Val Gly Ser Asp

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279/299

245										250					255				
Glu	Glu	Asp	Asp	Ser	Gly	Lys	Asp	Lys	Lys	Lys	Lys	Thr	Lys	Lys	Ile				
			260					265					270						
Lys	Glu	Lys	Tyr	Ile	Asp	Gln	Glu	Glu	Leu	Asn	Lys	Thr	Lys	Pro	Ile				
		275					280					285							
Trp	Thr	Arg	Asn	Pro	Asp	Asp	Ile	Thr	Gln	Glu	Glu	Tyr	Gly	Glu	Phe				
	290					295					300								
Tyr	Lys	Ser	Leu	Thr	Asn	Asp	Trp	Glu	Asp	His	Leu	Ala	Val	Lys	His				
305					310					315					320				
Phe	Ser	Val	Glu	Gly	Gln	Leu	Glu	Phe	Arg	Ala	Phe	Leu	Phe	Ile	Pro				
				325					330					335					
Arg	Arg	Ala	Pro	Phe	Asp	Leu	Phe	Glu	Asn	Lys	Lys	Lys	Lys	Asn	Asn				
			340					345						350					
Ile	Lys	Leu	Tyr	Val	Arg	Arg	Val	Phe	Ile	Met	Asp	Ser	Cys	Asp	Glu				
		355					360					365							
Leu	Ile	Pro	Glu	Tyr	Leu	Asn	Phe	Ile	Arg	Gly	Val	Val	Asp	Ser	Glu				
	370					375					380								
Asp	Leu	Pro	Leu	Asn	Ile	Ser	Arg	Glu	Met	Leu	Gln	Gln	Ser	Lys	Ile				
385					390					395					400				
Leu	Lys	Val	Ile	Arg	Lys	Asn	Ile	Val	Lys	Lys	Cys	Leu	Glu	Leu	Phe				
				405					410					415					
Ser	Glu	Leu	Ala	Glu	Asp	Lys	Glu	Asn	Tyr	Lys	Lys	Phe	Tyr	Glu	Ala				
			420					425					430						
Phe	Ser	Lys	Asn	Leu	Lys	Leu	Gly	Ile	His	Glu	Asp	Ser	Thr	Asn	Arg				
		435					440					445							
Arg	Arg	Leu	Ser	Glu	Leu	Leu	Arg	Tyr	His	Thr	Ser	Gln	Ser	Gly	Asp				
	450					455					460								
Glu	Met	Thr	Ser	Leu	Ser	Glu	Tyr	Val	Ser	Arg	Met	Lys	Glu	Thr	Gln				
465					470					475				480					
Lys	Ser	Ile	Tyr	Tyr	Ile	Thr	Gly	Glu	Ser	Lys	Glu	Gln	Val	Ala	Asn				
				485					490					495					
Pro	Ala	Phe	Val	Glu	Arg	Val	Arg	Lys	Arg	Gly	Phe	Glu	Val	Val	Tyr				
			500					505					510						
Met	Thr	Glu	Pro	Ile	Asp	Glu	Tyr	Cys	Val	Gln	Gln	Leu	Lys	Glu	Phe				
		515					520					525							
Asp	Gly	Lys	Ser	Leu	Val	Ser	Val	Thr	Lys	Glu	Gly	Leu	Glu	Leu	Pro				
	530					535					540								
Glu	Asp	Glu	Glu	Glu	Lys	Lys	Lys	Met	Glu	Glu	Ser	Lys	Ala	Lys	Phe				
545					550					555					560				

280/299

Glu Asn Leu Cys Lys Leu Met Lys Glu Ile Leu Asp Lys Lys Val Glu  
 565 570 575  
 Lys Val Thr Ile Ser Asn Arg Leu Val Ser Ser Pro Cys Cys Ile Val  
 580 585 590  
 Thr Ser Thr Tyr Gly Trp Thr Ala Asn Met Glu Arg Ile Met Lys Ala  
 595 600 605  
 Gln Ala Leu Arg Asp Asn Ser Thr Met Gly Tyr Met Met Ala Lys Lys  
 610 615 620  
 His Leu Glu Ile Asn Pro Asp His Pro Ile Val Glu Thr Leu Arg Gln  
 625 630 635 640  
 Lys Ala Glu Ala Asp Lys Asn Asp Lys Ala Val Lys Asp Leu Val Val  
 645 650 655  
 Leu Leu Phe Glu Thr Ala Leu Leu Ser Ser Gly Phe Ser Leu Glu Asp  
 660 665 670  
 Pro Gln Thr His Ser Asn Arg Ile Tyr Arg Met Ile Lys Leu Gly Leu  
 675 680 685  
 Gly Ile Asp Glu Asp Glu Val Thr Ala Glu Glu Pro Ser Ala Ala Val  
 690 695 700  
 Pro Asp Glu Ile Pro Pro Leu Glu Gly Asp Glu Asp Ala Ser Arg Met  
 705 710 715 720  
 Glu Glu Val Asp

<210> 322  
 <211> 724  
 <212> PRT  
 <213> Rattus sp.

<400> 322

Met Pro Glu Glu Val His His Gly Glu Glu Glu Val Glu Thr Phe Ala  
 1 5 10 15  
 Phe Gln Ala Glu Ile Ala Gln Leu Met Ser Leu Ile Ile Asn Thr Phe  
 20 25 30  
 Tyr Ser Asn Lys Glu Ile Phe Leu Arg Glu Leu Ile Ser Asn Ala Ser  
 35 40 45  
 Asp Ala Leu Asp Lys Ile Arg Tyr Glu Ser Leu Thr Asp Pro Ser Lys  
 50 55 60  
 Leu Asp Ser Gly Lys Glu Leu Lys Ile Asp Ile Ile Pro Asn Pro Gln  
 65 70 75 80  
 Glu Ala Thr Leu Thr Leu Val Asp Thr Gly Ile Gly Met Thr Lys Ala  
 85 90 95

281/299

Asp	Leu	Ile	Asn	Asn	Leu	Gly	Thr	Ile	Ala	Lys	Ser	Gly	Thr	Lys	Ala	100	105	110
Phe	Met	Glu	Ala	Leu	Gln	Ala	Gly	Ala	Asp	Ile	Ser	Met	Ile	Gly	Gln	115	120	125
Phe	Gly	Val	Gly	Phe	Tyr	Ser	Ala	Tyr	Leu	Val	Ala	Glu	Lys	Val	Val	130	135	140
Val	Ile	Thr	Lys	His	Asn	Asp	Asp	Glu	Gln	Tyr	Ala	Trp	Glu	Ser	Ser	145	150	155
Ala	Gly	Gly	Ser	Phe	Thr	Val	Arg	Ala	Asp	His	Gly	Glu	Pro	Ile	Gly	165	170	175
Arg	Gly	Thr	Lys	Val	Ile	Leu	His	Leu	Lys	Glu	Asp	Gln	Thr	Glu	Tyr	180	185	190
Leu	Glu	Glu	Arg	Arg	Val	Lys	Glu	Val	Val	Lys	Lys	His	Ser	Gln	Phe	195	200	205
Ile	Gly	Tyr	Pro	Ile	Thr	Leu	Tyr	Leu	Glu	Lys	Glu	Arg	Glu	Lys	Glu	210	215	220
Ile	Ser	Asp	Asp	Glu	Ala	Glu	Glu	Glu	Lys	Gly	Glu	Lys	Glu	Glu	Glu	225	230	235
Asp	Lys	Glu	Asp	Glu	Glu	Lys	Pro	Lys	Ile	Glu	Asp	Val	Gly	Ser	Asp	245	250	255
Glu	Glu	Asp	Asp	Ser	Gly	Lys	Asp	Lys	Lys	Lys	Lys	Thr	Lys	Lys	Ile	260	265	270
Lys	Glu	Lys	Tyr	Ile	Asp	Gln	Glu	Glu	Leu	Asn	Lys	Thr	Lys	Pro	Ile	275	280	285
Trp	Thr	Arg	Asn	Pro	Asp	Asp	Ile	Thr	Gln	Glu	Glu	Tyr	Gly	Glu	Phe	290	295	300
Tyr	Lys	Ser	Leu	Thr	Asn	Asp	Trp	Glu	Asp	His	Leu	Ala	Val	Lys	His	305	310	315
Phe	Ser	Val	Glu	Gly	Gln	Leu	Glu	Phe	Arg	Ala	Leu	Leu	Phe	Ile	Pro	325	330	335
Arg	Arg	Ala	Pro	Phe	Asp	Leu	Phe	Glu	Asn	Lys	Lys	Lys	Lys	Asn	Asn	340	345	350
Ile	Lys	Leu	Tyr	Val	Arg	Arg	Val	Phe	Ile	Met	Asp	Ser	Cys	Asp	Asp	355	360	365
Leu	Ile	Pro	Glu	Tyr	Leu	Asn	Phe	Ile	Arg	Gly	Val	Val	Asp	Ser	Glu	370	375	380
Asp	Leu	Pro	Leu	Asn	Ile	Ser	Arg	Glu	Met	Leu	Gln	Gln	Ser	Lys	Ile	385	390	395
Leu	Lys	Val	Ile	Arg	Lys	Asn	Ile	Val	Lys	Lys	Cys	Leu	Glu	Leu	Phe			



282/299

405					410					415					
Ser	Glu	Leu	Ala	Glu	Asp	Lys	Glu	Asn	Tyr	Lys	Lys	Phe	Tyr	Glu	Ala
			420					425					430		
Phe	Ser	Lys	Asn	Leu	Lys	Leu	Gly	Ile	His	Glu	Asp	Ser	Thr	Asn	Arg
		435					440					445			
Arg	Arg	Leu	Ser	Glu	Leu	Leu	Arg	Tyr	His	Thr	Ser	Gln	Ser	Gly	Asp
		450					455					460			
Glu	Met	Thr	Ser	Leu	Ser	Glu	Tyr	Val	Ser	Arg	Met	Lys	Glu	Thr	Gln
465						470					475				480
Lys	Ser	Ile	Tyr	Tyr	Ile	Thr	Gly	Glu	Ser	Lys	Glu	Gln	Val	Ala	Asn
			485						490					495	
Ser	Ala	Phe	Val	Glu	Arg	Val	Arg	Lys	Arg	Gly	Phe	Glu	Val	Val	Tyr
			500					505					510		
Met	Thr	Glu	Pro	Ile	Asp	Glu	Tyr	Cys	Val	Gln	Gln	Leu	Lys	Glu	Phe
		515					520					525			
Asp	Gly	Lys	Ser	Leu	Val	Ser	Val	Thr	Lys	Glu	Gly	Leu	Glu	Leu	Pro
	530					535					540				
Glu	Asp	Glu	Glu	Glu	Lys	Lys	Lys	Met	Glu	Glu	Ser	Lys	Ala	Arg	Phe
545						550					555				560
Glu	Asn	Leu	Cys	Lys	Leu	Met	Lys	Glu	Ile	Leu	Asp	Lys	Lys	Val	Glu
			565						570					575	
Lys	Val	Thr	Ile	Ser	Asn	Arg	Leu	Val	Ser	Ser	Pro	Cys	Cys	Ile	Val
			580					585					590		
Thr	Ser	Thr	Tyr	Gly	Trp	Thr	Ala	Asn	Met	Glu	Arg	Ile	Met	Lys	Ala
		595					600					605			
Gln	Ala	Leu	Arg	Asp	Asn	Ser	Thr	Met	Gly	Tyr	Met	Met	Ala	Lys	Lys
		610					615				620				
His	Leu	Glu	Ile	Asn	Pro	Asp	His	Pro	Ile	Val	Glu	Thr	Leu	Arg	Gln
625						630					635				640
Lys	Ala	Glu	Ala	Asp	Lys	Asn	Asp	Lys	Ala	Val	Lys	Asp	Leu	Val	Val
			645						650					655	
Leu	Leu	Phe	Glu	Thr	Ala	Leu	Ser	Ser	Leu	Ala	Ser	His	Phe	Arg	Arg
			660					665					670		
Pro	Lys	Thr	His	Ser	Asn	Arg	Ile	Tyr	Arg	Met	Ile	Lys	Leu	Gly	Leu
		675					680					685			
Gly	Ile	Asp	Glu	Asp	Glu	Val	Thr	Ala	Glu	Glu	Pro	Ser	Ala	Ala	Val
	690					695					700				
Pro	Asp	Glu	Ile	Pro	Pro	Leu	Glu	Gly	Asp	Glu	Asp	Ala	Ser	Arg	Met
705						710					715				720

283/299

Glu Glu Val Asp

&lt;210&gt; 323

&lt;211&gt; 733

&lt;212&gt; PRT

<213> *Cricetulus griseus*

&lt;400&gt; 323

Met	Pro	Glu	Glu	Thr	Gln	Thr	Gln	Asp	Gln	Pro	Met	Glu	Glu	Glu	Glu
1				5				10					15		
Val	Glu	Thr	Phe	Ala	Phe	Gln	Ala	Glu	Ile	Ala	Gln	Leu	Met	Ser	Leu
			20					25				30			
Ile	Ile	Asn	Thr	Phe	Tyr	Ser	Asn	Lys	Glu	Ile	Phe	Leu	Arg	Glu	Leu
		35					40					45			
Ile	Ser	Asn	Ser	Ser	Asp	Ala	Leu	Asp	Lys	Ile	Arg	Tyr	Glu	Ser	Leu
	50					55					60				
Thr	Asp	Pro	Ser	Lys	Leu	Asp	Ser	Gly	Lys	Glu	Leu	His	Ile	Asn	Ile
65					70					75					80
Ile	Pro	Asn	Lys	Gln	Asp	Arg	Thr	Leu	Thr	Ile	Val	Asp	Thr	Gly	Ile
				85					90					95	
Gly	Met	Thr	Lys	Ala	Asp	Leu	Ile	Asn	Asn	Leu	Gly	Thr	Ile	Ala	Lys
		100						105					110		
Ser	Gly	Thr	Lys	Ala	Phe	Met	Glu	Ala	Leu	Gln	Ala	Gly	Ala	Asp	Ile
		115					120					125			
Ser	Met	Ile	Gly	Gln	Phe	Gly	Val	Gly	Phe	Tyr	Thr	Ala	Tyr	Leu	Val
	130					135					140				
Ala	Glu	Lys	Val	Thr	Val	Ile	Thr	Lys	His	Asn	Asp	Asp	Glu	Gln	Tyr
145					150					155					160
Ala	Trp	Glu	Ser	Ser	Ala	Gly	Gly	Ser	Phe	Thr	Val	Arg	Thr	Asp	Thr
				165					170					175	
Gly	Glu	Pro	Met	Gly	Arg	Gly	Thr	Lys	Val	Ile	Leu	His	Leu	Lys	Glu
		180						185					190		
Asp	Gln	Thr	Glu	Tyr	Met	Glu	Glu	Arg	Arg	Ile	Lys	Glu	Ile	Val	Lys
		195					200					205			
Lys	His	Ser	Gln	Phe	Ile	Gly	Tyr	Pro	Ile	Thr	Leu	Phe	Val	Glu	Lys
	210					215					220				
Glu	Arg	Asp	Lys	Glu	Val	Ser	Asp	Asp	Glu	Ala	Glu	Glu	Lys	Glu	Asp
225					230					235					240
Lys	Glu	Glu	Glu	Lys	Glu	Lys	Glu	Glu	Lys	Gly	Ile	Asp	Asp	Lys	Pro
				245					250					255	

284/299

Glu Ile Glu Asp Val Gly Ser Asp Glu Glu Glu Glu Glu Lys Lys Asp  
 260 265 270  
 Gly Asp Lys Lys Lys Lys Lys Lys Ile Lys Glu Lys Tyr Ile Asp Gln  
 275 280 285  
 Glu Glu Leu Asn Lys Thr Lys Pro Ile Trp Thr Arg Asn Pro Asp Asp  
 290 295 300  
 Ile Thr Asn Glu Glu Tyr Gly Glu Phe Tyr Lys Ser Leu Thr Asn Asp  
 305 310 315 320  
 Trp Glu Glu His Leu Ala Val Lys His Phe Ser Val Glu Gly Gln Leu  
 325 330 335  
 Glu Phe Arg Ala Leu Leu Phe Val Pro Arg Arg Ala Pro Phe Asp Leu  
 340 345 350  
 Phe Glu Asn Arg Lys Lys Lys Asn Asn Ile Lys Leu Tyr Val Arg Arg  
 355 360 365  
 Val Phe Ile Met Asp Asn Cys Glu Glu Leu Phe Pro Glu Tyr Leu Asn  
 370 375 380  
 Phe Ile Arg Gly Val Val Asp Ser Glu Asp Leu Pro Leu Asn Ile Ser  
 385 390 395 400  
 Arg Glu Ile Leu Gln Gln Ser Lys Ile Leu Lys Val Ile Arg Lys Asn  
 405 410 415  
 Leu Val Arg Lys Cys Leu Glu Leu Phe His Glu Leu Ala Glu Asp Lys  
 420 425 430  
 Glu Asn Tyr Lys Lys Phe Tyr Glu Gln Phe Ser Lys Asn Ile Lys Leu  
 435 440 445  
 Gly Ile His Glu Asp Ser Gln Asn Arg Lys Lys Leu Ser Glu Leu Leu  
 450 455 460  
 Arg Tyr Tyr Thr Ser Ala Ser Gly Asp Glu Met Val Ser Leu Lys Asp  
 465 470 475 480  
 Tyr Cys Thr Arg Met Lys Glu Asn Gln Lys His Ile Tyr Phe Ile Thr  
 485 490 495  
 Gly Glu Thr Lys Asp Gln Val Ala Asn Ser Ala Phe Val Glu Arg Leu  
 500 505 510  
 Arg Lys His Gly Leu Glu Val Ile Tyr Met Ile Glu Pro Ile Asp Glu  
 515 520 525  
 Tyr Cys Val Gln Gln Leu Lys Glu Phe Glu Gly Lys Thr Leu Val Ser  
 530 535 540  
 Val Thr Lys Glu Gly Leu Glu Leu Pro Glu Asp Glu Glu Glu Lys Lys  
 545 550 555 560  
 Lys Gln Glu Glu Lys Lys Thr Lys Phe Glu Asn Leu Cys Lys Ile Met

285/299

565					570					575					
Lys	Asp	Ile	Leu	Glu	Lys	Lys	Val	Glu	Lys	Val	Val	Val	Ser	Asn	Arg
			580					585					590		
Leu	Val	Thr	Ser	Pro	Cys	Cys	Ile	Val	Thr	Ser	Thr	Tyr	Gly	Trp	Thr
		595					600					605			
Ala	Asn	Met	Glu	Arg	Ile	Ile	Lys	Ala	Gln	Ala	Leu	Arg	Asp	Asn	Ser
	610					615					620				
Thr	Met	Gly	Tyr	Met	Ala	Ala	Lys	Lys	His	Leu	Glu	Ile	Asn	Pro	Asp
625						630					635				640
His	Ser	Ile	Ile	Glu	Thr	Leu	Arg	Gln	Lys	Ala	Glu	Ala	Asp	Lys	Asn
				645					650					655	
Asp	Lys	Ser	Val	Lys	Asp	Leu	Val	Ile	Leu	Leu	Tyr	Glu	Thr	Ala	Leu
			660					665					670		
Leu	Ser	Ser	Gly	Phe	Ser	Leu	Glu	Asp	Pro	Gln	Thr	His	Ala	Asn	Arg
			675					680					685		
Ile	Tyr	Arg	Met	Ile	Lys	Leu	Gly	Leu	Gly	Ile	Asp	Glu	Asp	Asp	Pro
	690					695					700				
Thr	Val	Asp	Asp	Thr	Ser	Ala	Ala	Val	Thr	Glu	Glu	Met	Pro	Pro	Leu
705						710					715				720
Glu	Gly	Asp	Asp	Asp	Thr	Ser	Arg	Met	Glu	Glu	Val	Asp			
				725					730						

&lt;210&gt; 324

&lt;211&gt; 725

&lt;212&gt; PRT

&lt;213&gt; Gallus gallus

&lt;400&gt; 324

Met	Pro	Glu	Gln	Val	Gln	His	Gly	Glu	Asp	Glu	Val	Glu	Thr	Phe	Ala
1				5					10					15	
Phe	Gln	Ala	Glu	Ile	Ala	Gln	Leu	Met	Ser	Leu	Ile	Ile	Asn	Thr	Phe
			20					25					30		
Tyr	Ser	Asn	Lys	Glu	Ile	Phe	Leu	Arg	Glu	Leu	Ile	Ser	Asn	Ala	Ser
			35					40					45		
Asp	Ala	Leu	Asp	Lys	Ile	Arg	Tyr	Glu	Ser	Leu	Thr	Asp	Pro	Ser	Lys
	50					55					60				
Leu	Asp	Thr	Gly	Lys	Asp	Leu	Lys	Ile	Asp	Ile	Val	Pro	Asn	Pro	Arg
65						70					75				80
Asp	Pro	Thr	Leu	Thr	Leu	Leu	Asp	Thr	Gly	Ile	Gly	Met	Thr	Lys	Ala
				85					90					95	
Asp	Leu	Val	Asn	Asn	Leu	Gly	Thr	Ile	Ala	Lys	Ser	Gly	Thr	Lys	Ala

286/299

100					105					110					
Phe	Met	Glu	Ala	Leu	Gln	Ala	Gly	Ala	Asp	Ile	Ser	Met	Ile	Gly	Gln
		115					120					125			
Phe	Gly	Val	Gly	Phe	Tyr	Ser	Ala	Tyr	Leu	Val	Ala	Glu	Lys	Val	Val
	130					135					140				
Val	Ile	Thr	Lys	His	Asn	Asp	Asp	Glu	Gln	Tyr	Ala	Trp	Glu	Ser	Ser
145					150					155					160
Ala	Gly	Gly	Ser	Phe	Thr	Val	Arg	Thr	Asp	His	Gly	Glu	Pro	Ile	Gly
				165					170					175	
Arg	Gly	Thr	Lys	Val	Ile	Leu	Tyr	Leu	Lys	Glu	Asp	Gln	Thr	Glu	Tyr
			180					185					190		
Leu	Glu	Glu	Arg	Arg	Val	Lys	Glu	Val	Val	Lys	Lys	His	Ser	Gln	Phe
		195					200					205			
Ile	Gly	Tyr	Pro	Ile	Thr	Leu	Tyr	Val	Glu	Lys	Glu	Arg	Glu	Lys	Glu
	210					215					220				
Val	Ser	Asp	Asp	Glu	Ala	Glu	Glu	Glu	Lys	Val	Glu	Lys	Glu	Glu	Glu
225					230					235					240
Glu	Ser	Lys	Asp	Glu	Glu	Lys	Pro	Lys	Ile	Glu	Asp	Val	Gly	Ser	Asp
				245					250					255	
Glu	Glu	Glu	Glu	Glu	Gly	Glu	Lys	Ser	Lys	Lys	Lys	Lys	Thr	Lys	Lys
			260					265					270		
Ile	Lys	Glu	Lys	Tyr	Ile	Asp	Gln	Glu	Glu	Leu	Asn	Lys	Thr	Lys	Pro
		275					280					285			
Ile	Trp	Thr	Arg	Asn	Pro	Asp	Asp	Ile	Thr	Gln	Glu	Glu	Tyr	Gly	Glu
	290					295					300				
Phe	Tyr	Lys	Ser	Leu	Thr	Asn	Asp	Trp	Glu	Asp	His	Leu	Ala	Val	Lys
305					310					315					320
His	Phe	Ser	Val	Glu	Gly	Gln	Leu	Glu	Phe	Arg	Ala	Leu	Leu	Phe	Ile
				325					330					335	
Pro	Arg	Arg	Ala	Pro	Phe	Asp	Leu	Phe	Glu	Asn	Lys	Lys	Lys	Lys	Asn
			340					345					350		
Asn	Ile	Lys	Leu	Tyr	Val	Arg	Arg	Val	Phe	Ile	Met	Asp	Ser	Cys	Asp
	355					360						365			
Glu	Leu	Ile	Pro	Glu	Tyr	Leu	Asn	Phe	Ile	Arg	Gly	Val	Val	Asp	Ser
	370					375					380				
Glu	Asp	Leu	Pro	Leu	Asn	Ile	Ser	Arg	Glu	Met	Leu	Gln	Gln	Ser	Lys
385					390					395					400
Ile	Leu	Lys	Val	Ile	Arg	Lys	Asn	Ile	Val	Lys	Lys	Cys	Leu	Glu	Leu
				405					410					415	

Phe	Thr	Glu	Leu	Ala	Glu	Asp	Lys	Glu	Asn	Tyr	Lys	Lys	Phe	Tyr	Glu
			420					425					430		
Ala	Phe	Ser	Lys	Asn	Leu	Lys	Leu	Gly	Ile	His	Glu	Asp	Ser	Thr	Asn
		435					440					445			
Arg	Lys	Arg	Leu	Ser	Glu	Leu	Leu	Arg	Tyr	His	Thr	Ser	Gln	Ser	Gly
	450					455					460				
Asp	Glu	Met	Thr	Ser	Leu	Ser	Glu	Tyr	Val	Ser	Arg	Met	Lys	Glu	Ser
465					470					475					480
Gln	Lys	Ser	Ile	Tyr	Tyr	Ile	Thr	Gly	Glu	Ser	Lys	Glu	Gln	Val	Ala
			485						490					495	
Asn	Ser	Ala	Phe	Val	Glu	Arg	Val	Arg	Lys	Arg	Gly	Phe	Glu	Val	Val
			500					505					510		
Tyr	Met	Thr	Glu	Pro	Ile	Asp	Glu	Tyr	Cys	Val	Gln	Gln	Leu	Lys	Glu
		515					520					525			
Phe	Asp	Gly	Lys	Thr	Leu	Val	Ser	Val	Thr	Lys	Glu	Gly	Leu	Glu	Leu
	530					535					540				
Pro	Glu	Asp	Glu	Glu	Glu	Lys	Lys	Asn	Met	Glu	Glu	Ser	Lys	Ala	Lys
545					550					555					560
Phe	Glu	Thr	Leu	Cys	Lys	Leu	Met	Lys	Glu	Ile	Leu	Asp	Lys	Lys	Val
				565					570					575	
Glu	Lys	Val	Thr	Ile	Ser	Asn	Arg	Leu	Val	Ser	Ser	Pro	Cys	Cys	Ile
			580					585					590		
Val	Thr	Ser	Thr	Tyr	Gly	Trp	Thr	Ala	Asn	Met	Glu	Arg	Ile	Met	Lys
		595					600					605			
Ala	Gln	Ala	Leu	Arg	Asp	Asn	Ser	Thr	Met	Gly	Tyr	Met	Met	Ala	Lys
	610					615					620				
Lys	His	Leu	Glu	Ile	Asn	Pro	Asp	His	Pro	Ile	Val	Glu	Thr	Leu	Arg
625					630					635					640
Gln	Lys	Ala	Asp	Ala	Asn	Lys	Asn	Asp	Lys	Ala	Val	Lys	Asp	Leu	Val
				645					650					655	
Val	Leu	Leu	Phe	Glu	Thr	Ala	Leu	Leu	Ser	Ser	Gly	Phe	Ser	Leu	Glu
			660					665					670		
Asp	Pro	Gln	Thr	His	Ser	Asn	Arg	Ile	Tyr	Arg	Met	Ile	Lys	Leu	Gly
		675					680					685			
Leu	Gly	Ile	Asp	Glu	Asp	Glu	Val	Ile	Ala	Glu	Glu	Ser	Ser	Ile	Ala
	690					695					700				
Pro	Pro	Asp	Glu	Ile	Pro	Pro	Leu	Glu	Gly	Asp	Glu	Asp	Thr	Ser	Arg
705					710					715					720

288/299

Met Glu Glu Val Asp  
725

&lt;210&gt; 325

&lt;211&gt; 233

&lt;212&gt; PRT

<213> *Sarcophaga crassipalpis*

&lt;400&gt; 325

Phe Gly Val Gly Phe Tyr Ser Ala Tyr Leu Val Ala Asp Lys Val Thr  
1 5 10 15

Val Thr Ser Lys His Asn Asp Asp Glu Gln Tyr Ile Trp Glu Ser Ser  
20 25 30

Ala Gly Gly Ser Phe Thr Val Lys Pro Asp Ser Ser Glu Pro Leu Gly  
35 40 45

Arg Gly Thr Lys Ile Val Leu Tyr Ile Lys Glu Asp Gln Thr Glu Tyr  
50 55 60

Leu Glu Glu Ser Lys Ile Lys Glu Ile Val Asn Lys His Ser Gln Phe  
65 70 75 80

Ile Gly Tyr Pro Ile Lys Leu Leu Val Gln Lys Glu Arg Asp Gln Glu  
85 90 95

Val Ser Asp Asp Glu Ala Glu Glu Glu Lys Lys Glu Met Asp Thr Asp  
100 105 110

Glu Pro Lys Ile Glu Asp Val Gly Glu Asp Glu Asp Ala Asp Lys Lys  
115 120 125

Asp Lys Asp Gly Lys Lys Lys Lys Thr Ile Lys Val Ala Tyr Thr Glu  
130 135 140

Asp Glu Glu Leu Asn Lys Thr Lys Pro Ile Trp Thr Arg Asn Pro Asp  
145 150 155 160

Asp Ile Thr Gln Ala Glu Tyr Gly Asp Phe Tyr Lys Ser Leu Thr Asn  
165 170 175

Asp Trp Glu Asp His Leu Ala Val Lys His Phe Pro Leu Lys Gly Gln  
180 185 190

Leu Glu Phe Arg Ala Leu Leu Phe Ile Pro Arg Arg Thr Pro Phe Asp  
195 200 205

Leu Phe Glu Asn Gln Lys Lys Arg Asn Asn Ile Lys Leu Tyr Val Pro  
210 215 220

Arg Val Phe Ile Met Asp Asn Cys Glu  
225 230

&lt;210&gt; 326

&lt;211&gt; 724

289/299

&lt;212&gt; PRT

&lt;213&gt; Danio rerio

&lt;400&gt; 326

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Met Pro Glu Glu Met Arg Gln Glu Glu Glu Ala Glu Thr Phe Ala Phe
  1           5           10           15

Gln Ala Glu Ile Ala Gln Leu Met Ser Leu Ile Ile Asn Thr Phe Tyr
      20           25           30

Ser Asn Lys Glu Ile Phe Leu Arg Glu Leu Val Ser Asn Ala Ser Asp
      35           40           45

Ala Leu Asp Lys Ile Arg Tyr Glu Ser Leu Thr Asp Pro Thr Lys Leu
      50           55           60

Asp Ser Gly Lys Asp Leu Lys Ile Asp Ile Ile Pro Asn Val Gln Glu
      65           70           75           80

Arg Thr Leu Thr Leu Ile Asp Thr Gly Ile Gly Met Thr Lys Ala Asp
      85           90           95

Leu Ile Asn Asn Leu Gly Thr Ile Ala Lys Ser Gly Thr Lys Ala Phe
      100          105          110

Met Glu Ala Leu Gln Ala Gly Ala Asp Ile Ser Met Ile Gly Gln Phe
      115          120          125

Gly Val Gly Phe Tyr Ser Ala Tyr Leu Val Ala Glu Lys Val Thr Val
      130          135          140

Ile Thr Lys His Asn Asp Asp Glu Gln Tyr Ala Trp Glu Ser Ser Ala
      145          150          155          160

Gly Gly Ser Phe Thr Val Lys Val Asp His Gly Glu Pro Ile Gly Arg
      165          170          175

Gly Thr Lys Val Ile Leu His Leu Lys Glu Asp Gln Thr Glu Tyr Ile
      180          185          190

Glu Glu Lys Arg Val Lys Glu Val Val Lys Lys His Ser Gln Phe Ile
      195          200          205

Gly Tyr Pro Ile Thr Leu Tyr Val Glu Lys Glu Arg Asp Lys Glu Ile
      210          215          220

Ser Asp Asp Glu Ala Glu Glu Glu Lys Ala Glu Lys Glu Glu Lys Glu
      225          230          235          240

Glu Glu Gly Glu Asp Lys Pro Lys Ile Glu Asp Val Gly Ser Asp Asp
      245          250          255

Glu Glu Asp Thr Lys Asp Lys Asp Lys Lys Lys Lys Lys Lys Ile Lys
      260          265          270

Glu Lys Tyr Ile Asp Gln Glu Glu Leu Asn Lys Thr Lys Pro Ile Trp
      275          280          285

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290/299

Thr Arg Asn Pro Asp Asp Ile Ser Asn Glu Glu Tyr Gly Glu Phe Tyr  
 290 295 300  
 Lys Ser Leu Thr Asn Asp Trp Glu Asp His Leu Ala Val Lys His Phe  
 305 310 315 320  
 Ser Val Glu Gly Gln Leu Glu Phe Arg Ala Leu Leu Phe Ile Pro Arg  
 325 330 335  
 Arg Ala Pro Phe Asp Leu Phe Glu Asn Lys Lys Lys Lys Asn Asn Ile  
 340 345 350  
 Lys Leu Tyr Val Arg Arg Val Phe Ile Met Asp Asn Cys Glu Glu Leu  
 355 360 365  
 Ile Pro Glu Tyr Leu Asn Phe Ile Arg Gly Val Val Asp Ser Glu Asp  
 370 375 380  
 Leu Pro Leu Asn Ile Ser Arg Glu Met Leu Gln Gln Ser Lys Ile Leu  
 385 390 395 400  
 Lys Val Ile Arg Lys Asn Ile Val Lys Lys Cys Leu Glu Leu Phe Ala  
 405 410 415  
 Asp Val Ala Glu Asp Lys Asp Asn Tyr Lys Lys Phe Tyr Asp Ala Phe  
 420 425 430  
 Ser Lys Asn Leu Lys Leu Gly Ile His Glu Asp Ser Gln Asn Arg Arg  
 435 440 445  
 Lys Leu Ser Glu Leu Leu Arg Tyr Gln Ser Ser Gln Ser Gly Tyr Glu  
 450 455 460  
 Met Thr Ser Leu Thr Glu Tyr Val Ser Arg Met Lys Glu Asn Gln Lys  
 465 470 475 480  
 Ser Ile Tyr Tyr Ile Thr Gly Glu Ser Lys Asp Gln Val Ala His Ser  
 485 490 495  
 Ala Phe Val Glu Arg Val Cys Lys Arg Gly Phe Glu Val Leu Tyr Met  
 500 505 510  
 Thr Glu Pro Ile Asp Glu Tyr Cys Val Gln Gln Leu Lys Asp Phe Asp  
 515 520 525  
 Gly Lys Ser Leu Val Ser Val Thr Lys Glu Gly Leu Glu Leu Pro Glu  
 530 535 540  
 Asp Glu Asp Glu Lys Lys Lys Met Glu Glu Asp Lys Ala Lys Phe Glu  
 545 550 555 560  
 Asn Leu Cys Lys Leu Met Lys Glu Ile Leu Asp Lys Lys Val Glu Lys  
 565 570 575  
 Val Thr Val Ser Asn Arg Leu Val Ser Ser Pro Cys Cys Ile Val Thr  
 580 585 590  
 Ser Thr Tyr Gly Trp Thr Ala Asn Met Glu Arg Ile Met Lys Ala Gln

291/299

595	600	605
Ala Leu Arg Asp Asn Ser Thr Met Gly Tyr Met Met Ala Lys Lys His		
610	615	620
Leu Glu Ile Asn Pro Asp His Pro Ile Met Glu Thr Leu Arg Gln Lys		
625	630	635
Ala Glu Ala Asp Lys Asn Asp Lys Ala Val Lys Asp Leu Val Ile Leu		
645	650	655
Leu Phe Glu Thr Ala Leu Leu Ser Ser Gly Phe Ser Leu Asp Asp Pro		
660	665	670
Gln Thr His Ser Asn Arg Ile Tyr Arg Met Ile Lys Leu Gly Leu Gly		
675	680	685
Ile Asp Glu Asp Glu Asp Val Pro Val Glu Glu Pro Ser Ser Ala Ala		
690	695	700
Pro Glu Asp Ile Pro Pro Leu Glu Gly Asp Asp Asp Ala Ser Arg Met		
705	710	715
		720
Glu Glu Val Asp		

&lt;210&gt; 327

&lt;211&gt; 722

&lt;212&gt; PRT

&lt;213&gt; Salmo salar

&lt;400&gt; 327

Met Pro Glu Glu Met Arg Gln Glu Glu Glu Ala Glu Thr Phe Ala Phe
1 5 10 15
Gln Ala Glu Ile Ala Gln Leu Met Ser Leu Ile Ile Asn Thr Phe Tyr
20 25 30
Ser Asn Lys Glu Ile Phe Leu Arg Glu Leu Ile Ser Asn Ala Ser Asp
35 40 45
Ala Leu Asp Lys Ile Arg Tyr Glu Ser Leu Thr Asp Pro Thr Lys Leu
50 55 60
Asp Asn Gly Lys Glu Leu Lys Ile Asp Val Ile Pro Asn Val Glu Glu
65 70 75 80
Arg Thr Leu Thr Leu Ile Asp Thr Gly Ile Gly Met Thr Lys Ala Asp
85 90 95
Leu Ile Asn Asn Leu Gly Thr Ile Ala Lys Ser Gly Thr Lys Ala Phe
100 105 110
Met Glu Ala Leu Gln Ala Gly Ala Asp Ile Ser Met Ile Gly Gln Phe
115 120 125
Gly Val Gly Phe Tyr Ser Ala Tyr Leu Val Ala Glu Arg Val Thr Val
130 135 140

292/299

Ile	Thr	Lys	His	Asn	Asp	Asp	Glu	Gln	Tyr	Ile	Trp	Glu	Ser	Ser	Ala	145	150	155	160
Gly	Gly	Ser	Phe	Thr	Val	Lys	Val	Asp	Thr	Gly	Glu	Pro	Met	Leu	Arg	165	170	175	
Gly	Thr	Lys	Val	Ile	Leu	His	Met	Lys	Glu	Asp	Gln	Thr	Glu	Tyr	Val	180	185	190	
Glu	Glu	Lys	Arg	Val	Lys	Glu	Val	Val	Lys	Lys	His	Ser	Gln	Phe	Ile	195	200	205	
Gly	Tyr	Pro	Ile	Thr	Leu	Phe	Val	Glu	Lys	Glu	Arg	Glu	Lys	Glu	Ile	210	215	220	
Ser	Asp	Asp	Glu	Glu	Glu	Lys	Ala	Glu	Glu	Glu	Lys	Glu	Glu	Lys	Glu	225	230	235	240
Ala	Glu	Asp	Lys	Pro	Lys	Ile	Glu	Asp	Val	Gly	Ser	Asp	Asp	Glu	Glu	245	250	255	
Asp	Ser	Lys	Asp	Lys	Asp	Lys	Lys	Lys	Thr	Lys	Lys	Ile	Lys	Glu	Lys	260	265	270	
Tyr	Ile	Asp	Gln	Glu	Glu	Leu	Asn	Lys	Thr	Lys	Pro	Ile	Trp	Thr	Arg	275	280	285	
Asn	Pro	Asp	Asp	Ile	Thr	Met	Glu	Glu	Tyr	Gly	Glu	Phe	Tyr	Lys	Ser	290	295	300	
Leu	Thr	Asn	Asp	Trp	Glu	Glu	His	Leu	Ala	Val	Lys	His	Phe	Ser	Val	305	310	315	320
Glu	Gly	Gln	Leu	Glu	Phe	Arg	Ala	Leu	Leu	Phe	Ile	Pro	Arg	Arg	Ala	325	330	335	
Pro	Phe	Asp	Leu	Phe	Glu	Asn	Lys	Lys	Lys	Lys	Asn	Asn	Ile	Lys	Leu	340	345	350	
Tyr	Val	Arg	Arg	Val	Phe	Ile	Met	Asp	Ser	Cys	Glu	Glu	Leu	Ile	Pro	355	360	365	
Glu	Tyr	Leu	Asn	Phe	Val	Arg	Gly	Val	Val	Asp	Ser	Glu	Asp	Leu	Pro	370	375	380	
Leu	Asn	Ile	Ser	Arg	Glu	Met	Leu	Gln	Gln	Ser	Lys	Ile	Leu	Lys	Val	385	390	395	400
Ile	Arg	Lys	Asn	Ile	Val	Lys	Lys	Cys	Met	Glu	Leu	Phe	Gly	Glu	Leu	405	410	415	
Ala	Glu	Asp	Arg	Glu	Asn	Tyr	Asn	Lys	Phe	Tyr	Asp	Gly	Phe	Ser	Lys	420	425	430	
Asn	Leu	Lys	Leu	Gly	Ile	His	Glu	Asp	Ser	Gln	Asn	Arg	Lys	Lys	Leu	435	440	445	

293/299

Ser Glu Leu Leu Arg Tyr His Ser Ser Gln Ser Gly Asp Glu Leu Thr  
 450 455 460  
 Ser Leu Thr Glu Tyr Leu Thr Arg Met Lys Asp Asn Gln Lys Ser Ile  
 465 470 475 480  
 Tyr Tyr Ile Thr Gly Glu Ser Lys Asp Gln Val Ala Asn Ser Ala Phe  
 485 490 495  
 Val Glu Arg Val Arg Lys Arg Gly Phe Glu Val Leu Tyr Met Thr Glu  
 500 505 510  
 Pro Ile Asp Glu Tyr Cys Val Gln Gln Leu Lys Glu Phe Asp Gly Lys  
 515 520 525  
 Thr Leu Val Ser Val Thr Lys Glu Gly Leu Glu Leu Pro Glu Asp Glu  
 530 535 540  
 Glu Glu Lys Lys Lys Met Asp Glu Asp Lys Thr Lys Phe Glu Asn Leu  
 545 550 555 560  
 Cys Lys Leu Met Lys Glu Ile Leu Asp Lys Lys Val Glu Lys Val Thr  
 565 570 575  
 Val Ser Asn Arg Leu Val Ser Ser Pro Cys Cys Ile Val Thr Ser Thr  
 580 585 590  
 Tyr Gly Trp Thr Ala Asn Met Glu Arg Ile Met Lys Ala Gln Ala Leu  
 595 600 605  
 Arg Asp Asn Ser Thr Met Gly Tyr Met Met Ala Lys Lys His Leu Glu  
 610 615 620  
 Ile Asn Pro Asp His Pro Ile Val Glu Thr Leu Arg Gln Lys Ala Asp  
 625 630 635 640  
 Leu Asp Lys Asn Asp Lys Ala Val Lys Asp Leu Val Ile Leu Leu Phe  
 645 650 655  
 Glu Thr Ala Leu Leu Ser Ser Gly Phe Ser Leu Asp Asp Pro Gln Thr  
 660 665 670  
 His Ser Asn Arg Ile Tyr Arg Met Ile Lys Leu Gly Leu Gly Ile Asp  
 675 680 685  
 Asp Asp Glu Val Ile Pro Glu Glu Pro Thr Ser Ala Pro Ala Pro Asp  
 690 695 700  
 Glu Ile Pro Pro Leu Glu Gly Asp Asp Asp Ala Ser Arg Met Glu Glu  
 705 710 715 720

Val Asp

&lt;210&gt; 328

&lt;211&gt; 733

&lt;212&gt; PRT

&lt;213&gt; Sus scrofa

294/299

&lt;400&gt; 328

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Met Pro Glu Glu Thr Gln Thr Gln Asp Gln Pro Met Glu Glu Glu Glu
 1           5           10           15

Val Glu Thr Phe Ala Phe Gln Ala Glu Ile Ala Gln Leu Met Ser Leu
      20           25           30

Ile Ile Asn Thr Phe Tyr Ser Asn Lys Glu Ile Phe Leu Arg Glu Leu
      35           40           45

Ile Ser Asn Ser Ser Asp Ala Leu Asp Lys Ile Arg Tyr Glu Ser Leu
      50           55           60

Thr Asp Pro Ser Lys Leu Asp Ser Gly Lys Glu Leu His Ile Asn Leu
      65           70           75           80

Ile Pro Asn Lys Gln Asp Arg Thr Leu Thr Ile Val Asp Thr Gly Ile
      85           90           95

Gly Met Thr Lys Ala Asp Leu Ile Asn Asn Leu Gly Thr Ile Ala Lys
      100          105          110

Ser Gly Thr Lys Ala Phe Met Glu Ala Leu Gln Ala Gly Ala Asp Ile
      115          120          125

Ser Met Ile Gly Gln Phe Gly Val Gly Phe Tyr Ser Ala Tyr Leu Val
      130          135          140

Ala Glu Lys Val Thr Val Ile Thr Lys His Asn Asp Asp Glu Gln Tyr
      145          150          155          160

Ala Trp Glu Ser Ser Ala Gly Gly Ser Phe Thr Val Arg Thr Asp Thr
      165          170          175

Gly Glu Pro Met Gly Arg Gly Thr Lys Val Ile Leu His Leu Lys Glu
      180          185          190

Asp Gln Thr Glu Tyr Leu Glu Glu Arg Arg Ile Lys Glu Ile Val Lys
      195          200          205

Lys His Ser Gln Phe Ile Gly Tyr Pro Ile Thr Leu Phe Val Glu Lys
      210          215          220

Glu Arg Asp Lys Glu Val Ser Asp Asp Glu Ala Glu Glu Lys Glu Asp
      225          230          235          240

Lys Glu Glu Glu Lys Glu Lys Glu Glu Lys Glu Ser Glu Asp Lys Pro
      245          250          255

Glu Ile Glu Asp Val Gly Ser Asp Glu Glu Glu Glu Glu Lys Lys Asp
      260          265          270

Gly Asp Lys Lys Lys Lys Lys Lys Ile Lys Glu Lys Tyr Ile Asp Gln
      275          280          285

Glu Glu Leu Asn Lys Thr Lys Pro Ile Trp Thr Arg Asn Pro Asp Asp
      290          295          300

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295/299

Ile	Thr	Asn	Glu	Glu	Tyr	Gly	Glu	Phe	Tyr	Lys	Ser	Leu	Thr	Asn	Asp		
305					310					315					320		
Trp	Glu	Asp	His	Leu	Ala	Val	Lys	His	Phe	Ser	Val	Glu	Gly	Gln	Leu		
				325					330					335			
Glu	Phe	Arg	Ala	Leu	Leu	Phe	Val	Pro	Arg	Arg	Ala	Pro	Phe	Asp	Leu		
			340					345					350				
Phe	Glu	Asn	Arg	Lys	Lys	Lys	Asn	Asn	Ile	Lys	Leu	Tyr	Val	Arg	Arg		
		355					360					365					
Val	Phe	Ile	Met	Asp	Asn	Cys	Glu	Glu	Leu	Ile	Pro	Glu	Tyr	Leu	Asn		
	370					375					380						
Phe	Ile	Arg	Gly	Val	Val	Asp	Ser	Glu	Asp	Leu	Pro	Leu	Asn	Ile	Ser		
385					390					395					400		
Arg	Glu	Met	Leu	Gln	Gln	Ser	Lys	Ile	Leu	Lys	Val	Ile	Arg	Lys	Asn		
			405						410					415			
Leu	Val	Lys	Lys	Cys	Leu	Glu	Leu	Phe	Thr	Glu	Leu	Ala	Glu	Asp	Lys		
			420					425					430				
Glu	Asn	Tyr	Lys	Lys	Phe	Tyr	Glu	Gln	Phe	Ser	Lys	Asn	Ile	Lys	Leu		
		435					440					445					
Gly	Ile	His	Glu	Asp	Ser	Gln	Asn	Arg	Lys	Lys	Leu	Ser	Glu	Leu	Leu		
	450					455					460						
Arg	Tyr	Tyr	Thr	Ser	Ala	Ser	Gly	Asp	Glu	Met	Val	Ser	Leu	Lys	Asp		
465					470					475					480		
Tyr	Cys	Thr	Arg	Met	Lys	Glu	Asn	Gln	Lys	His	Ile	Tyr	Tyr	Ile	Thr		
				485					490					495			
Gly	Glu	Thr	Lys	Asp	Gln	Val	Ala	Asn	Ser	Ala	Phe	Val	Glu	Arg	Leu		
			500					505					510				
Arg	Lys	His	Gly	Leu	Glu	Val	Ile	Tyr	Met	Ile	Glu	Pro	Ile	Asp	Glu		
		515					520					525					
Tyr	Cys	Val	Gln	Gln	Leu	Lys	Glu	Phe	Glu	Gly	Lys	Thr	Leu	Val	Ser		
		530				535					540						
Val	Thr	Lys	Glu	Gly	Leu	Glu	Leu	Pro	Glu	Asp	Glu	Glu	Glu	Lys	Lys		
545					550					555					560		
Lys	Gln	Glu	Glu	Lys	Lys	Thr	Lys	Phe	Glu	Asn	Leu	Cys	Lys	Ile	Met		
				565					570					575			
Lys	Asp	Ile	Leu	Glu	Lys	Lys	Val	Glu	Lys	Val	Val	Val	Ser	Asn	Arg		
			580					585					590				
Leu	Val	Thr	Ser	Pro	Cys	Cys	Ile	Val	Thr	Ser	Thr	Tyr	Gly	Trp	Thr		
		595					600					605					

296/299

Ala Asn Met Glu Arg Ile Met Lys Ala Gln Ala Leu Arg Asp Asn Ser  
 610 615 620

Thr Met Gly Tyr Met Ala Ala Lys Lys His Leu Glu Ile Asn Pro Asp  
 625 630 635 640

His Ser Ile Ile Glu Thr Leu Arg Gln Lys Ala Glu Ala Asp Lys Asn  
 645 650 655

Asp Lys Ser Val Lys Asp Leu Val Ile Leu Leu Tyr Glu Thr Ala Leu  
 660 665 670

Leu Ser Ser Gly Phe Ser Leu Glu Asp Pro Gln Thr His Ala Asn Arg  
 675 680 685

Ile Tyr Arg Met Ile Lys Leu Gly Leu Gly Ile Asp Glu Asp Asp Pro  
 690 695 700

Thr Ala Asp Asp Ser Ser Ala Ala Val Thr Glu Glu Met Pro Pro Leu  
 705 710 715 720

Glu Gly Asp Asp Asp Thr Ser Arg Met Glu Glu Val Asp  
 725 730

&lt;210&gt; 329

&lt;211&gt; 709

&lt;212&gt; PRT.

<213> *Saccharomyces cerevisiae*

&lt;400&gt; 329

Met Ala Ser Glu Thr Phe Glu Phe Gln Ala Glu Ile Thr Gln Leu Met  
 1 5 10 15

Ser Leu Ile Ile Asn Thr Val Tyr Ser Asn Lys Glu Ile Phe Leu Arg  
 20 25 30

Glu Leu Ile Ser Asn Ala Ser Asp Ala Leu Asp Lys Ile Arg Tyr Lys  
 35 40 45

Ser Leu Ser Asp Pro Lys Gln Leu Glu Thr Glu Pro Asp Leu Phe Ile  
 50 55 60

Arg Ile Thr Pro Lys Pro Glu Gln Lys Val Leu Glu Ile Arg Asp Ser  
 65 70 75 80

Gly Ile Gly Met Thr Lys Ala Glu Leu Ile Asn Asn Leu Gly Thr Ile  
 85 90 95

Ala Lys Ser Gly Thr Lys Ala Phe Met Glu Ala Leu Ser Ala Gly Ala  
 100 105 110

Asp Val Ser Met Ile Gly Gln Phe Gly Val Gly Phe Tyr Ser Leu Phe  
 115 120 125

Leu Val Ala Asp Arg Val Gln Val Ile Ser Lys Ser Asn Asp Asp Glu  
 130 135 140

297/299

Gln Tyr Ile Trp Glu Ser Asn Ala Gly Gly Ser Phe Thr Val Thr Leu  
 145 150 155 160  
 Asp Glu Val Asn Glu Arg Ile Gly Arg Gly Thr Ile Leu Arg Leu Phe  
 165 170 175  
 Leu Lys Asp Asp Gln Leu Glu Tyr Leu Glu Glu Lys Arg Ile Lys Glu  
 180 185 190  
 Val Ile Lys Arg His Ser Glu Phe Val Ala Tyr Pro Ile Gln Leu Val  
 195 200 205  
 Val Thr Lys Glu Val Glu Lys Glu Val Pro Ile Pro Glu Glu Glu Lys  
 210 215 220  
 Lys Asp Glu Glu Lys Lys Asp Glu Glu Lys Lys Asp Glu Asp Asp Lys  
 225 230 235 240  
 Lys Pro Lys Leu Glu Glu Val Asp Glu Glu Glu Lys Lys Pro Lys  
 245 250 255  
 Thr Lys Lys Val Lys Glu Glu Val Gln Glu Ile Glu Glu Leu Asn Lys  
 260 265 270  
 Thr Lys Pro Leu Trp Thr Arg Asn Pro Ser Asp Ile Thr Gln Glu Glu  
 275 280 285  
 Tyr Asn Ala Phe Tyr Lys Ser Ile Ser Asn Asp Trp Glu Asp Pro Leu  
 290 295 300  
 Tyr Val Lys His Phe Ser Val Glu Gly Gln Leu Glu Phe Arg Ala Ile  
 305 310 315 320  
 Leu Phe Ile Pro Lys Arg Ala Pro Phe Asp Leu Phe Glu Ser Lys Lys  
 325 330 335  
 Lys Lys Asn Asn Ile Lys Leu Tyr Val Arg Arg Val Phe Ile Thr Asp  
 340 345 350  
 Glu Ala Glu Asp Leu Ile Pro Glu Trp Leu Ser Phe Val Lys Gly Val  
 355 360 365  
 Val Asp Ser Glu Asp Leu Pro Leu Asn Leu Ser Arg Glu Met Leu Gln  
 370 375 380  
 Gln Asn Lys Ile Met Lys Val Ile Arg Lys Asn Ile Val Lys Lys Leu  
 385 390 395 400  
 Ile Glu Ala Phe Asn Glu Ile Ala Glu Asp Ser Glu Gln Phe Glu Lys  
 405 410 415  
 Phe Tyr Ser Ala Phe Ser Lys Asn Ile Lys Leu Gly Val His Glu Asp  
 420 425 430  
 Thr Gln Asn Arg Ala Ala Leu Ala Lys Leu Leu Arg Tyr Asn Ser Thr  
 435 440 445  
 Lys Ser Val Asp Glu Leu Thr Ser Leu Thr Asp Tyr Val Thr Arg Met



298/299

450	455	460
Pro Glu His Gln Lys Asn Ile Tyr Tyr Ile Thr Gly Glu Ser Leu Lys 465	470	475
Ala Val Glu Lys Ser Pro Phe Leu Asp Ala Leu Lys Ala Lys Asn Phe 485	490	495
Glu Val Leu Phe Leu Thr Asp Pro Ile Asp Glu Tyr Ala Phe Thr Gln 500	505	510
Leu Lys Glu Phe Glu Gly Lys Thr Leu Val Asp Ile Thr Lys Asp Phe 515	520	525
Glu Leu Glu Glu Thr Asp Glu Glu Lys Ala Glu Arg Glu Lys Glu Ile 530	535	540
Lys Glu Tyr Glu Pro Leu Thr Lys Ala Leu Lys Glu Ile Leu Gly Asp 545	550	555
Gln Val Glu Lys Val Val Val Ser Tyr Lys Leu Leu Asp Ala Pro Ala 565	570	575
Ala Ile Arg Thr Gly Gln Phe Gly Trp Ser Ala Asn Met Glu Arg Ile 580	585	590
Met Lys Ala Gln Ala Leu Arg Asp Ser Ser Met Ser Ser Tyr Met Ser 595	600	605
Ser Lys Lys Thr Phe Glu Ile Ser Pro Lys Ser Pro Ile Ile Lys Glu 610	615	620
Leu Lys Lys Arg Val Asp Glu Gly Gly Ala Gln Asp Lys Thr Val Lys 625	630	635
Asp Leu Thr Lys Leu Leu Tyr Glu Thr Ala Leu Leu Thr Ser Gly Phe 645	650	655
Ser Leu Asp Glu Pro Thr Ser Phe Ala Ser Arg Ile Asn Arg Leu Ile 660	665	670
Ser Leu Gly Leu Asn Ile Asp Glu Asp Glu Glu Thr Glu Thr Ala Pro 675	680	685
Glu Ala Ser Thr Ala Ala Pro Val Glu Glu Val Pro Ala Asp Thr Glu 690	695	700
Met Glu Glu Val Asp 705		

&lt;210&gt; 330

&lt;211&gt; 260

&lt;212&gt; PRT

&lt;213&gt; Rana esculenta

&lt;400&gt; 330

Glu Met Ala Ser Leu Ser Glu Tyr Val Ser Arg Met Lys Glu Thr Gln

299/299

1	5	10	15
Lys Ser Ile Tyr Tyr Ile Thr Gly Glu Ser Lys Glu Gln Val Ala Asn	20	25	30
Ser Ala Phe Val Glu Arg Val Arg Lys Arg Gly Phe Glu Val Val Tyr	35	40	45
Met Thr Glu Pro Ile Asp Glu Tyr Cys Val Gln Gln Leu Lys Glu Phe	50	55	60
Asp Gly Lys Thr Leu Val Ser Val Thr Lys Glu Gly Leu Glu Leu Pro	65	70	75
Glu Asp Asp Glu Glu Lys Lys Lys Met Glu Glu Asn Lys Thr Lys Phe	85	90	95
Glu Gly Leu Cys Lys Leu Met Lys Glu Ile Leu Asp Lys Lys Val Glu	100	105	110
Lys Val Thr Val Ser Asn Arg Leu Val Ser Ser Pro Cys Cys Ile Val	115	120	125
Thr Ser Thr Tyr Gly Trp Thr Ala Asn Met Glu Arg Ile Met Lys Ala	130	135	140
Gln Ala Leu Arg Asp Asn Ser Thr Met Gly Tyr Met Met Ala Lys Lys	145	150	155
His Leu Glu Ile Asn Pro Glu His Pro Ile Val Glu Thr Leu Arg Gln	165	170	175
Lys Ala Glu Ala Asp Lys Asn Asp Lys Ala Val Lys Asp Leu Val Val	180	185	190
Leu Leu Phe Glu Thr Ala Leu Leu Ser Ser Gly Phe Ser Leu Asp Asp	195	200	205
Pro Gln Thr His Ser Asn Arg Ile Tyr Arg Met Ile Lys Leu Gly Leu	210	215	220
Gly Ile Asp Glu Asp Glu Pro Ala Ile Glu Glu Thr Thr Ala Ala Val	225	230	235
Pro Asp Asp Ile Pro Pro Leu Glu Gly Glu Glu Asp Ala Ser Arg Met	245	250	255
Glu Glu Val Asp	260		

**DERWENT-ACC-NO:** 2002-698710**DERWENT-WEEK:** 200817*COPYRIGHT 2010 DERWENT INFORMATION LTD*

**TITLE:** Treating genetically-defined disease associated with chromosomal aberrations yielding oncogenic fusion proteins, e.g. cell proliferative diseases, involves administering an inhibitor of heat shock protein 90

**INVENTOR:** BURROWS F; BURROWS F J ; FRITZ L ; FRITZ L  
C

**PATENT-ASSIGNEE:** BURROWS F[BURRI] , CONFORMA  
THERAPEUTIC CORP[CONFN] , CONFORMA  
THERAPEUTICS CORP[CONFN] , FRITZ L  
[FRITI]

**PRIORITY-DATA:** 2001US-272751P (March 1, 2001) ,  
2002WO-US06518 (March 1, 2002) ,  
2003US-469469 (August 27, 2003) ,  
2007US-779243 (July 17, 2007)

**PATENT-FAMILY:**

<b>PUB-NO</b>	<b>PUB-DATE</b>	<b>LANGUAGE</b>
WO 02069900 A2	September 12, 2002	EN
AU 2002252179 A1	September 19, 2002	EN
EP 1423080 A2	June 2, 2004	EN
US 20060079493 A1	April 13, 2006	EN
AU 2002252179 A8	October 27, 2005	EN
US 20080051462 A1	February 28, 2008	EN

**DESIGNATED-STATES:** AE AG AL AM AT AU AZ BA BB BG BR  
 BY BZ CA CH CN CO CR CU CZ DE DK  
 DM DZ EC EE ES FI GB GD GE GH GM  
 HR HU ID IL IN IS JP KE KG KP KR  
 KZ LC LK LR LS LT LU LV MA MD MG  
 MK MN MW MX MZ NO NZ OM PH PL PT  
 RO RU SD SE S G SI SK SL TJ TM TN  
 TR TT TZ UA UG US UZ VN YU ZA ZM  
 ZW AT BE CH CY DE DK EA ES FI FR  
 GB GH GM GR IE IT KE LS LU MC MW  
 MZ NL OA PT SD SE SL SZ TR TZ UG  
 ZM ZW AL AT BE CH CY DE DK ES FI  
 FR GB GR IE IT LI LT LU LV MC MK  
 NL PT RO SE SI TR

**APPLICATION-DATA:**

<b>PUB-NO</b>	<b>APPL-DESCRIPTOR</b>	<b>APPL-NO</b>	<b>APPL-DATE</b>
WO2002069900A2	N/A	2002WO- US06518	March 1, 2002
AU2002252179A1	N/A	2002AU- 252179	March 1, 2002
AU2002252179A8	N/A	2002AU- 252179	March 1, 2002
EP 1423080A2	N/A	2002EP- 721238	March 1, 2002
EP 1423080A2	N/A	2002WO- US06518	March 1, 2002
US20060079493A1	N/A	2002WO- US06518	March 1, 2002
US20060079493A1	N/A	2003US- 469469	August 27, 2003
US20080051462A1	Based on	2007US- 779243	July 17, 2007

**INT-CL-CURRENT:**

<b>TYPE</b>	<b>IPC DATE</b>
CIPP	A61K31/135 20060101
CIPP	A61K31/33 20060101
CIPS	A61K31/395 20060101
CIPS	A61P35/00 20060101
CIPS	A61P43/00 20060101
CIPS	C12P21/08 20060101
CIPS	C12Q1/68 20060101
CIPS	G01N33/53 20060101

**ABSTRACTED-PUB-NO:** WO 02069900 A2

**BASIC-ABSTRACT:**

NOVELTY - Treating (M) genetically-defined disease associated with chromosomal aberrations yielding oncogenic fusion proteins (I), treating cancerous cells containing (I) in a heterogeneous cell population, treating proliferative diseases (PD) associated with mutant protein or cellular protein isoforms (II) dependent on heat shock protein (HSP)-90, or selectively treating cells expressing (II), involves administering HSP90-inhibitor.

DESCRIPTION - A method (M) comprising:

(a) treating a patient having a genetically-defined disease characterized by a chromosomal aberration that yields an oncogenic fusion protein, by providing a cell, tissue or fluid sample of a patient suspected of having the genetically-defined disease, identifying one or more characteristics indicative of the disease

in or on the cell, tissue or fluid sample, and administering to the patient, a pharmaceutically effective amount of HSP90-inhibiting compound (III);

(b) treating cancerous cells in a heterogeneous population of cells (the heterogeneous population comprises both cancerous and non-cancerous cells and cancerous cells being characterized by fusion proteins not found in noncancerous cells), by administering a pharmaceutically effective amount of (III) to the heterogeneous population of cells;

(c) treating a patient having a proliferative disease associated with a mutant protein or cellular protein isoform (II) dependent on HSP90, by providing a cell, tissue, or fluid sample of a patient suspected of having the proliferative disease, identifying in the cell, tissue, or fluid sample one or more characteristics indicative of (II), and administering a pharmaceutically effective amount of (III) to the patient; or

(d) selectively treating cells that express (II) that gives to a proliferative disorder dependent on HSP90, by providing a population of cells in which at least some of the population express (II) that is differentially dependent on HSP90 for effect and gives rise to a proliferative disorder, and administering a pharmaceutically effective amount of (III) to the population.

HSP-90 inhibitor (claimed).

USE - (M) Is useful for treating genetically-defined disease with chromosomal aberration yielding oncogenic fusion protein, treating cancerous cells containing fusion protein in heterogeneous cell population, treating proliferative disease (e.g. rheumatoid arthritis or cancer) associated with mutant protein or

cellular protein isoform dependent on heat shock protein (HSP)-90 (e.g. p53), or selectively treating cells expressing mutant protein or cellular protein isoform in a patient heterozygous for (II).

(M) Is useful for treating a disease e.g. hematopoietic disorder such as T or B cell lymphoma, chronic myeloid leukemia (CML), APL, ALL, AML, NHL and CMML, or a disease characterized by a solid tumor such as papillary thyroid carcinoma, Ewing's sarcoma, melanoma, liposarcoma, rhabdomyosarcoma and synovial sarcoma (claimed).

(M) is also useful for treating viral infections.

## **EQUIVALENT-ABSTRACTS:**

### BIOTECHNOLOGY

Preferred Compound: (III) Is ansamycin e.g. geldanamycin, 17-AAG, herbimycin A and macbecin, or radicicol or its analog. (III) binds into the ATP-binding site of a HSP90.

Preferred Method: (M) Further involves identifying a nucleic acid encoding (I), by using polymerase chain reaction (PCR) or ligase chain reaction (LCR), using an antibody to identify (I), or using a cytochemical technique which employs nucleic acid hybridization (e.g. fluorescence in situ hybridization (FISH)). (I) contains one or more functional domains or their portions of kinases and DNA binding motifs. The method is an ex vivo method.

(III) Has an IC(50) at least 2-10 fold higher for cells that do not have characteristics indicative of the genetically-defined proliferative disorder relative to those cells that do have such characteristics. The cells of the patient are

monitored in vitro for sensitivity prior to administration of (III) to the patient. The non-random chromosomal aberration is translocation, inversion or deletion. The non-random chromosomal aberration is selected from any one of the aberrations given in the specification, e.g. t(9;22)(q34;q11) optionally characterized by and comprising a sequence of 63, 63, 423, 222, 1079 or 106 nucleotides fully defined in the specification (encoding a sequence of 21, 21, 140, 307, 359 or 34 amino acids fully defined in the specification), or its homolog, isoform or allelic variant.

Alternately, (III) has an IC(50) that is at least 5-10 fold lower for the cancerous cells than for the noncancerous cells within heterogeneous population, and where the pharmaceutically effective amount administered is about half or less of the IC(50) of the noncancerous cells. Treatment is monitored by PCR, antibody staining or nucleic acid hybridization, which are selective for the presence of cancerous cells.

(I) Has a heightened dependence on HSP90.

(III) Is a synthetic analog of geldanamycin.

(II) is src, RET, p53, p51, p63, p73, or their homologs and allelic variations. (II) is a dominant negative mutant, e.g. human p53 such as N239S, C176R, and R213asterisk, Y236DELTA, C176Y, M133T, G245D, E258K, 1-293 DELTA, G245C, R248W, E258K, R282W, R175HU, R280K, V143A, R175H, P177S, H178P, H179R, R181P, 138-9DELTA, G245S, G245D, M246R, R248Q, R249S, R273H, R273C, R273L, and D218Y.

Alternately, (II) is a dominant positive mutant or a C176Y mutant.

(III) Is administered through intralesional or



parenteral route (claimed).

(III) is administered at a dose of 0.01-100 mg/kg body weight, preferably 0.1-10 mg/kg body weight.

**TITLE-TERMS:** TREAT GENETIC DEFINE DISEASE ASSOCIATE  
CHROMOSOME ABERRATION YIELD ONCOGENIC  
FUSE PROTEIN CELL PROLIFERATION  
ADMINISTER INHIBIT HEAT SHOCK

**DERWENT-CLASS:** B04 B05 D16

**CPI-CODES:** B04-B04C2; B04-C01G; B04-E03F; B04-E05;  
B04-G01; B04-N02A0E; B11-A02; B11-C07A;  
B11-C08E; B11-C08F; B11-C08G; B12-K04A1;  
B14-C06; B14-C09; B14-H01; B14-S03; D05-A02B;  
D05-H07; D05-H08; D05-H09; D05-H11; D05-H12A;  
D05-H12D1; D05-H18; D05-H18B;

**CHEMICAL-CODES:** Chemical Indexing M1 \*06\*  
Fragmentation Code M423 M750 N102  
N134 N152 Q233 Specific Compounds  
RA00NS Registry Numbers 93605

Chemical Indexing M1 \*07\*  
Fragmentation Code M423 M750 N102  
N134 N152 Q233 Specific Compounds  
RA012P Registry Numbers 105730

Chemical Indexing M1 \*08\*  
Fragmentation Code M417 M423 M430  
M782 N102 N134 N152 P831 Q233 Q505  
Specific Compounds RA013I Registry  
Numbers 184610

Chemical Indexing M1 \*09\*  
Fragmentation Code M423 M430 M782  
N102 N134 N152 P831 Q233 Q505  
Specific Compounds RA031J Registry

Numbers 204310 204644

Chemical Indexing M1 \*10\*  
Fragmentation Code M417 M423 M781  
N102 P831 Q233 Q505 Specific  
Compounds RA00C8 Registry Numbers  
184587

Chemical Indexing M1 \*11\*  
Fragmentation Code M417 M423 M750  
N102 Q233 Specific Compounds RA00H1  
Registry Numbers 184611

Chemical Indexing M1 \*12\*  
Fragmentation Code M417 M423 M750  
N102 Q233 Specific Compounds RA00H3  
Registry Numbers 184616

Chemical Indexing M1 \*13\*  
Fragmentation Code M417 M423 M750  
N102 N136 Q233 Specific Compounds  
RA00GT Registry Numbers 200757 200799

Chemical Indexing M2 \*01\*  
Fragmentation Code D015 D021 D023  
D030 D041 E570 F011 F014 F022 F433 H1  
H181 H2 H201 H4 H403 H422 H441 H5  
H521 H8 J0 J011 J2 J221 J5 J522 J561  
K0 L9 L941 L951 M210 M211 M214 M232  
M240 M262 M272 M273 M281 M283 M320  
M412 M511 M521 M530 M540 M781 P421  
P423 P631 P633 Q233 Ring Index  
Numbers 47063 47155 Specific  
Compounds R18825 Registry Numbers  
105651

Chemical Indexing M2 \*02\*  
Fragmentation Code D015 D024 D690 H4  
H401 H421 H5 H522 H541 H8 J5 J521

J522 K0 L4 L463 L9 L941 L951 M210  
M211 M240 M272 M283 M320 M412 M511  
M520 M530 M540 M781 P421 P423 P631  
P633 Q233 Ring Index Numbers 47148  
Specific Compounds RA0V2E Registry  
Numbers 95974

Chemical Indexing M2 \*03\*  
Fragmentation Code D015 D024 D690 H1  
H102 H141 H4 H401 H421 H5 H522 H7  
H716 H721 H8 J5 J521 J522 K0 L4 L463  
L9 L941 L951 M210 M211 M213 M231 M240  
M272 M273 M281 M282 M283 M320 M412  
M511 M520 M530 M540 M781 P421 P423  
P631 P633 Q233 Ring Index Numbers  
47148 Specific Compounds RA2AFE  
Registry Numbers 162868

Chemical Indexing M2 \*04\*  
Fragmentation Code D015 D024 D690 H5  
H523 H541 H8 J5 J521 J522 K0 L4 L463  
L9 L941 L951 M210 M211 M240 M272 M283  
M320 M412 M511 M520 M530 M540 M781  
P421 P423 P631 P633 Q233 Ring Index  
Numbers 47148 Specific Compounds  
RA2RSN Registry Numbers 334393

Chemical Indexing M2 \*05\*  
Fragmentation Code D014 D024 D230 H4  
H402 H442 H6 H602 H641 H8 J5 J522 L9  
L942 M210 M211 M240 M281 M320 M412  
M511 M520 M530 M540 M781 P421 P423  
P631 P633 Q233 Ring Index Numbers  
51839 Specific Compounds R04889  
Registry Numbers 101246

Chemical Indexing M6 \*14\*  
Fragmentation Code P421 P423 P631  
P633 P831 Q233 Q505 R231 R502 R515

R520 R521 R614 R621 R624 R627 R631  
R637 R639

**SECONDARY-ACC-NO:**

**CPI Secondary Accession Numbers:** 2002-197903